Original Article

Assessment on the Effects of Hepatitis B Prevention and Control Measures in Western China: A Comparison of Three Population-based Serosurveys*

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Abstract

Objective Despite the remarkable progress in efforts to control disease spread, the nationwide elimination of hepatitis B in China is still hindered by the persistently high rate of hepatitis B virus (HBV) infection in Western China. This study aimed to evaluate the strategy of hepatitis B prevention and control in Western China and identify potential areas and strategies for improvement.

Methods Susceptible population vaccination, health education, professional training of doctors, and other prevention and control measures have been implemented in Wuwei city since 2010. Data were obtained from three representative cross-sectional serosurveys conducted in 2010, 2013, and 2015. The serum samples were subjected to enzyme-linked immunosorbent assays to detect the following seromarkers: HBV surface antigen (HBsAg), antibody against hepatitis B surface antigen (anti-HBs), and antibody against hepatitis B core antigen (anti-HBc). Estimates of variance were determined using Taylor series linearization methods.

Results The three serosurveys revealed decreases in the prevalence of HBsAg (7.19% in 2010 *vs.* 6.51% in 2013 *vs.* 5.87% in 2015) and anti-HBc positivity (43.89% *vs.* 32.87% *vs.* 28.46%) and an increase in the prevalence of anti-HBs positivity (49.07% *vs.* 53.66% *vs.* 53.72%) over time. From 2010 to 2015, the legally reported incidence of hepatitis B in Wuwei city decreased from 686.53/100,000 to 53.72/100,000. Notably, persistently high HBsAg-positive rates (above 5.40%) were observed among subjects aged 20–69 years old in the three serosurveys; the prevalence of HBsAg was above 1% among children younger than 10 years old. Furthermore, rural subjects had higher rates of HBsAg and anti-HBc positivity than their urban counterparts (6.04% *vs.* 4.83% and 30.26% *vs.* 20.35%, respectively) in 2015 but had a lower rate of anti-HBs positivity (49.68 *vs.* 55.18%). Multivariate regression analysis showed that age, urban and rural areas, and education level were the main factors affecting HBV infection.

Conclusion Although vaccine-based prevention and control measures reduced the rate of HBV infection in Wuwei City over time, the hepatitis B infection rate in children younger than 10 years was still higher than the national average level. Therefore, the prevention and control of mother-to-child transmission and the management of the infected should be the focus of future prevention and control work.

Key words: Hepatitis B; Prevention and control measures; Serosurvey; Western China

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INTRODUCTION

Hepatitis B is an infectious disease mainly caused by hepatitis B virus (HBV). This disease places heavy economic burdens on patients, their families, and societies. An estimated total of 300,000 people die of hepatitis B-related liver cancer or cirrhosis every year, accounting for 37%–50% of all hepatitis B-related deaths worldwide[1,2]. In Asia, China is considered an intermediate-to-high hepatitis B-endemic region[3].

Since its initial inclusion in the national immunization program in 1992, the hepatitis B vaccine has led to a significant decrease in the prevalence of HBV infection in China. Particularly, the positive rate of HBV surface antigen (HBsAg) has decreased to < 1% among children younger than 10 years[4]. A recent meta-analysis revealed that the rate of HBsAg positivity in the general Chinese population (age range: 1–59 years) was 5.7%, a 20.61% decline from the rate of 7.18% recorded 10 years earlier in 2006[5]. Moreover, data from the Statutory Infectious Diseases Report indicate that the incidence of hepatitis B in China decreased from 89.00/100,000 in 2007 to 68.74/100,000 in 2016[6]. Despite these decreases, the population of HBsAg carriers continually exceeds 80 million residents due to the highly populous nature of China. Therefore, the prevention and control of hepatitis B in China will have a considerable impact on the global elimination of viral hepatitis[7-9].

Although China has made remarkable progress in controlling the spread of HBV by expanding infant immunization programs, efforts to eliminate this virus in the country have been limited, mainly due to regional imbalances in infection. According to the results of a national serosurvey conducted in 2006, the prevalence of HBsAg in Western China remained as high as 8.2%[4]. Although no national HBV serosurvey was conducted on the whole population between 2006 and 2019, a recent meta-analysis of HBV infection reported the highest rate in Western China [8.92%; 95% confidence interval (*CI*): 7.19%–10.64%][10]. The resistance to viral elimination in this region poses the greatest challenge to the goal of nationwide viral hepatitis eradication in 2030[11]. Consequently, Western China has become the focus of national hepatitis B prevention and treatment efforts.

Wuwei, located in the middle of Gansu province, is the eastern gate of Silk Road into Hexi Corridor and Xinjiang. This typical agricultural city in Western China is characterized by a multi-ethnic and largely rural population, poor economic conditions, underdeveloped medical and health facilities, a large number of migrant workers, and high population mobility. The incidence of hepatitis B in Wuwei increased from 571/100,000 in 2005 to 742/100,000 in 2008, which is eight times higher than the national average according to National Disease Supervision Information Management System (NDSIMS)[12].

To prevent and control the HBV spread, the Ministry of Science and Technology of China developed demonstration areas in seven locations, including Wuwei city, in 2008. In 2009, the project of hepatitis B prevention and control demonstration area in Wuwei was launched. A cross-sectional survey of the prevalence of hepatitis B in Wuwei in 2010 revealed HBV infection rates of 7.19% and 8.56% among people older than 1 year of age and among rural adults, respectively[13]. These rates were significantly higher than those reported in a nationwide hepatitis B epidemiological survey conducted in 2006[4]. In summary, HBV infection represents a serious public health issue faced by the residents of Wuwei and Western China. Since 2009, special funds have been provided to enable the implementation of a series of prevention and control measures, including vaccination, health education, and specialized training for physicians, in Western China. This study was to compare the results of three serosurveys conducted in 2010, 2013, and 2015 in the Wuwei hepatitis B prevention and control demonstration area. Specifically, this study aimed to evaluate the effects of specific hepatitis B prevention and control measures and to provide the most recent data in support of further improvements to these measures in Western China.

METHODS

Study Population and Sampling Methods

The three surveys were conducted from January 2010 to March 2010, from January 2013 to May 2013, and from September 2015 to December 2015. The research object was defined as the whole population of Wuwei, and the same serosurvey sampling method was adopted in 2010[13], 2013, and 2015. The minimum sampling unit was a village or subdistrict. Therefore, the rural population comprised subjects whose minimum residential unit was a village, whereas the urban population consisted of those whose minimum residential unit was a subdistrict.

Investigation

All serosurveys used similar methods and questionnaires. All investigators were trained by professionals at the Air Force Medical University and designated as official investigators after passing an examination. The investigators conducted face-to-face interviews of each subject (or designated guardian) in accordance with the method of centralized and household entry investigation, with assistance from the local township health centers, village committees, and other departments. A standardized questionnaire survey method was used to collect basic information, including gender, date of birth, education level (for those older than 15 years), ethnicity, residential area, and HBV immunization history, from the respondents.

HBsAg positive was defined as HBV infection. HBV infection case records pertaining to Wuwei were obtained *via* the Legal Infectious Disease Surveillance System. Three serum surveys were conducted using population data (including gender and age) from the 2010 national Census of Wuwei city (see Supplementary Table S1 available in www.besjournal.com). Data corresponding to the total population of China from 2010 to 2015 were obtained from the World Bank (https://data.worldbank.org.cn/). National hepatitis B incidence data were obtained from NDSIMS.

Laboratory Testing

Sera were collected from the subjects' blood samples (5 mL) and stored at −80 °C. Enzyme-linked immunosorbent assays (Yantai Laboratory System, Beijing, China) were used to screen the serum samples for HBsAg, anti-HBs, and anti-HBc.

Data Analysis

Data were entered into EpiData 3.1 software (EpiData Association, Odense, Denmark) and analyzed using SAS 9.2 statistical software (SAS Institute, Cary, NC, USA). The complex sampling design was based on Taylor series linearization method, and the standard errors were estimated accurately. The calculated prevalence rates of HBV markers were weighted based on gender, age, ethnicity and occupation, and other selected determinants to account for differences in the selected probabilities across subdistricts, communities, and villages and between age and gender categories. The weight for each person, i, is expressed as follows:

$$W_{kji} = \frac{W_i}{W_k \times W_{j|k}} \tag{1}$$

where i refers to the respondents; W_k and $W_{j|k}$ represent the sampling probabilities of the county and village, respectively; W_i denotes the adjustment factor for person i (based on the age and gender composition of the 2010 Wuwei Census data). The survey data from 2013 were divided on the basis of the age groups used in the 2010 hepatitis B serosurvey in Wuwei city to facilitate direct comparisons. Both data sets were adjusted based on the age and gender composition of the population of Wuwei city based on the 2010 Census.

The prevalence rates of HBV seromarkers were reported as point estimates and estimated 95% *CI*s. The latter ranges were compared when contrasting the prevalence rates of each seromarker, such that 95% *CI*s that did not overlap between groups were considered statistically significant (P < 0.05). Changing trends in the prevalence rates were calculated using the chi-square test. Multivariate unconditional logistic regression model was used to analyze the factors influencing HBV infection. With HBsAg positive as the dependent variable and multiple research factors (including gender, age, race, education level, urban and rural areas) as independent variables, a multi-factor regression analysis was conducted. The age group is divided into two groups: those over 14 years old and those under 14 years old; The ethnicity are divided into han nationality and minority nationality; Gender, age, race, urban and rural data were dichotomous variables. Education is an unordered variable, assigned a value of 1 to 4.

Ethical Considerations

The study protocol was approved by the Ethics Committee of the Air Force Medical University. Consent to participate in the survey was obtained from all participants or their parents/guardians (for minor children). Specifically, each participant or their parent/guardian signed an informed consent form and also provided written consent on the first page of the questionnaire.

RESULTS

HBV Prevention and Control Measures in Wuwei from 2010 to 2015

By 2015, the overall HBV immunization rate was 99.87%, and the rate of timely first vaccination among newborn infants was 96.71%. Moreover, 85.64%, 82.71%, and 82.16% of middle school students, primary school students, and residents in this area, respectively, reported an awareness of hepatitis B and health education, indicating that the project had yielded significant social benefits. The rate of awareness about hepatitis B prevention and treatment among community physicians who served rural populations increased from 67% before the intervention to above 81% upon its completion (Table 1).

Characteristics of the Participants in the 2010, 2013, and 2015 Serosurveys

Overall, 28,044, 35,232, and 20,358 samples were analyzed in the 2010, 2013, and 2015 serosurveys, with male-to-female ratios of 0.77:1, 0.93:1, and 0.81:1, respectively. All serosurvey populations included similar distributions of age groups, ethnic groups, education levels (among those older than 15 years), and urban and rural residents. Table 2 shows the demographic characteristics of the three groups.

Overall Prevalence of HBV Serological Markers in 2010, 2013, and 2015

A serological investigation conducted in Wuwei in 2010 yielded HBsAg, anti-HBs, and anti-HBc positivity rates of 7.19% (95% *CI*: 6.28%–8.11%), 49.07% (95% *CI*: 45.50%–52.65%), and 43.89% (95% *CI*: 40.37%–47.41%), respectively. In 2013, the corresponding rates for HBsAg, anti-HBs, and anti-HBc positivity were 6.51% (95% *CI*: 6.29%–6.73%), 53.66% (95% *CI*: 52.42%–54.91%), and 32.87% (95% *CI*: 31.43%–34.30%), respectively. In 2015, the corresponding positivity rates were 5.87% (HBsAg, 95% *CI*: 5.41%–6.25%), 53.72% (anti-HBs, 95% *CI*: 50.27%–55.78%), and 28.46% (anti-HBc, 95% *CI*: 26.42%–30.65%). Compared with 2010, the positive rate of anti-HBs in 2015 was significantly increased, while the positive rates of HBsAg and anti-HBc were significantly decreased ($P < 0.05$; Table 3).

Age-specific Positive Rate of HBV Seromarkers in 2010, 2013, and 2015

The rates of HBsAg, anti-HBs, and anti-HBc positivity differed significantly between age groups ($P < 0.05$). In 2010, the rate of HBsAg seropositivity increased with age, peaking at 8.72% in the age group of 40–49 years, and declined. In 2013, the rate of HBsAg seropositivity increased with age, peaking at 8.57% in the age group of 50–59 years and decreasing to 7.76% and 4.96% in those aged 60–69 and ≥ 70 years, respectively. In 2015, the rate of HBsAg seropositivity increased with age, peaking at 7.47% in the 60–69-year-old age group and decreasing to 6.42% in those aged in ≥ 70 years. Despite these fluctuations, all rates of HBsAg positivity among adults aged 20–69 years remained higher than 5.46%. Moreover, the HBsAg seropositive rate of children aged 0–9 years was over 1% in 2010 (1.91%), 2013 (1.78%), and 2015 (1.24%). Compared with the data of 2010, except for the 10–19-year-old age group, the serum positive rate of HBsAg in other age groups was not statistically significant in 2015 (Figure 1A).

The results demonstrated a decrease in the rate of anti-HBs seropositivity with age. In 2010, the highest rate of anti-HBs positivity (53.26%) was observed among people aged 10–19 years, followed

Table 1. HBV prevention and control measures applied in Wuwei city in 2010–2015

Measures	Respondents	Index
Free vaccination	Children, adults	Vaccination of 294,943 residents: 75,561 newborns, 53,111 susceptible adults, 26,649 members of high-risk and key groups (e.g., hospital medical staff and families of HBsAg-positive individuals), 1,138 rural doctors, and 137,820 people younger than 15 years.
Health education and knowledge promotion	Residents	A total of 304 hepatitis B prevention and control slogans (10,000 m^2); A total of 920,000 SMS sent monthly to all mobile phone users; Production of hepatitis B prevention and control public service advertisements for rolling broadcasts four times per day; Printing and distribution of 50,000 health education posters, 26,000 copies of hepatitis B prevention and control information manuals, 20,000 copies of hepatitis B prevention and control leaflets, two types of Health Education Prescriptions (10,000 copies), 10,000 copies of medical institution posters, 20,000 copies of publicity calendars, 8,000 publicity handbags, 10,000 publicity pens, and 105 coloring/drawing publicity pages.
Physician training	Clinicians, managing physicians, village and community physicians	Training of 1,022 clinicians and managing physicians in infectious disease at public health departments in township (or higher-level) hospitals, and 2107 rural and community-level physicians (total = 3,129), with 100% training coverage.

by that among adolescents (50.76%) aged 0–9 years. The positive rate of anti-HBs in other age groups was between 40% and 50%. In 2013, the highest rate of anti-HBs positivity (63.92%) was observed among people aged 10–19 years, followed by that in adults aged 20–29 years (56.93%). All other age groups had anti-HBs positivity rate of approximately 50%. In 2015, the positive rate of anti-HBs was over 50% in all age groups, with the highest value recorded in the population aged 0–9 years (62.37%) followed by the 10–19-year-old group (59.56%). Compared with the data of 2010, except for the 0–9 and 40–49-year-old age groups, the positive rate of anti-HBs in other age groups was significantly higher in 2013 and 2015 ($P < 0.05$) (Figure 1B). Furthermore, we analyzed the positive rate of anti-HBs at 1–5 years old in 2013 and 2015, and found that the anti-HBs positive rate in children aged 1–5 years were 70.00%, 71.79%, 60.53%, 43.46%, and 42.98%. The rate was significantly the highest among children aged 2 years and decreased thereafter (χ^2= 26.27, $P < 0.01$) (see Supplementary Table S2 available in www.besjournal.com).

The three serosurveys showed that the rate of anti-HBc seropositivity also increased with age. Compared with the data of 2010, the rates of anti-

Table 2. Characteristics of the study populations in the 2010, 2013, and 2015 serosurveys

Category	2010		2013		2015	
	Frequency	Proportion (%)	Frequency	Proportion (%)	Frequency	Proportion (%)
Overall	28,044	100.00	35,232	100.00	20,358	100.00
Age (years)						
0–9	1,649	5.88	2,532	7.19	1,076	5.28
10–19	4,844	17.27	5,204	14.77	4,251	20.88
20–59	17,535	62.53	23,312	66.17	12,157	59.72
≥ 60	4,016	14.32	4,184	11.87	2,874	14.12
Gender						
Male	12,218	43.57	16,939	48.08	9,090	44.65
Female	15,826	56.43	18,293	51.92	11,268	55.35
Ethnicity						
Han	26,515	94.55	33,611	95.40	19,068	93.66
Uighur	263	0.94	296	0.84	159	0.78
Tibetan	990	3.53	1,207	3.43	857	4.21
Others	276	0.98	118	0.33	274	1.35
Education (subjects aged 15–59 years)						
Illiterate or primary school	8,125	40.51	9,981	38.08	4,335	34.17
Middle school	7,239	36.10	11,146	42.52	4,947	38.99
High school	3,397	16.94	3,521	13.43	1,671	13.17
Junior college or undergraduate degree	1,294	6.45	1,566	5.97	1,735	13.67
Urban/rural						
Urban	6,092	21.72	8,768	24.89	5,221	25.65
Rural	21,952	78.28	26,464	75.11	15,137	74.35

Table 3. Rates of HBV serological marker seropositivity in the 2010, 2013, and 2015 survey populations

Year	HBsAg (%) (95% *CI*)	Anti-HBs (%) (95% *CI*)	Anti-HBc (%) (95% *CI*)
2010	7.19 (6.28–8.11)	49.07 (45.50–52.65)	43.89 (40.37–47.71)
2013	6.51 (6.29–6.73)	53.66 (52.42–54.91)	32.87 (31.43–34.30)
2015	5.87 (5.41–6.31)	53.72 (50.27–55.78)	28.46 (26.42–30.65)

HBc seropositivity decreased in subjects aged 10 years or older (P < 0.05). However, the positive rate of anti-HBc in adults over 20 years old remained at a high level, especially in the age group over 40 years, i.e., above 30% (Figure 1C).

Rates of HBV Marker Positivity Stratified by Gender, Ethnicity, Education Level, and Residential Area

In an analysis stratified by gender, male subjects had higher rates of HBsAg positivity than female

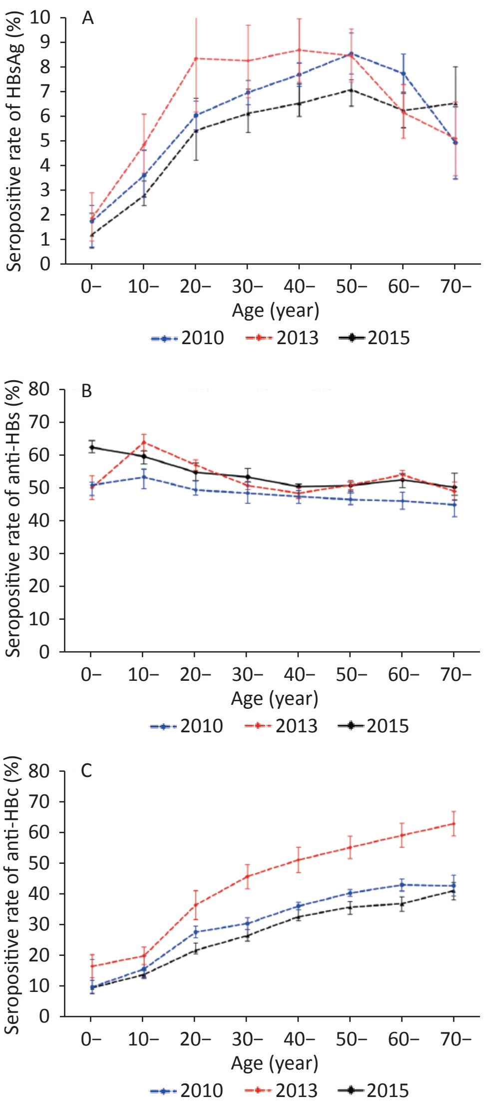

Figure 1. Rates of HBV seromarker seropositivity stratified by age group in 2010, 2013, and 2015 survey populations. Bars indicate the 95% *CI*. (A) Comparison of HBsAg seropositivity. (B) Comparison of anti-HBs seropositivity. (C) Comparison of anti-HBc seropositivity.

subjects in the three serosurveys, but the difference was not statistically significant (P > 0.05). The prevalence of anti-HBc decreased, whereas the positive rate of anti-HBs increased in 2010–2015 (P < 0.05). In particular, the prevalence rates of HBsAg and anti-HBc decreased in 2015 compared with 2010 among males and females, but a statistically significant decrease was identified only for HBsAg prevalence in males (Table 3).

In an analysis stratified by ethnicity, the participants of Han ethnicity had higher rates of HBsAg positivity than those from Tibetan, Uighur, and other ethnic groups in the three serosurveys. However, the participants of Uighur ethnicity had the highest rate of anti-HBs positivity. The rates of anti-HBc positivity were highest in the Han group and lowest in the Uighur group in 2013 and 2015. In the three serosurveys, the rates of anti-HBc positivity decreased significantly in the Han and Uighur groups, whereas the rates of anti-HBs positivity increased significantly (P < 0.05; Table 4).

In an analysis stratified by education level, the results of the three surveys revealed that the rate of HBsAg positivity decreased as the education level increased, with the highest and lowest rates observed in the groups with junior middle school education and junior college or higher education, respectively. Moreover, with the rise in educational level, the rates of anti-HBs and anti-HBc positivity increased and decreased, respectively. The results obtained in both surveys were generally similar, although the rates of anti-HBc and anti-HBs positivity significantly decreased and increased, respectively, from 2010 to 2015 (Table 4).

In an analysis stratified by area of residence, the three surveys demonstrated lower rates of HBsAg and anti-HBc positivity and higher rates of anti-HBs positivity in urban areas than in rural areas (P > 0.05). Compared with 2010, the rates of HBsAg and anti-HBc positivity decreased in urban and rural areas in 2013 and in 2015, although only the latter was significant (P < 0.05). Moreover, the rates of anti-HBs positivity increased significantly over time in urban and rural areas (P < 0.05; Table 4).

We also analyzed the factors that may affect HBV infection, such as sex, age, ethnicity, urban and rural areas, education, etc. The results showed that age, urban and rural areas, and education were the main factors influencing HBV infection. Among the factors influencing HBV infection, the *OR* value estimates of male and female in 2010, 2013, and 2015 were 1.32, 1.26, and 1.22, which indicated that after excluding other factors, the probability of HBV infection in

Table 4. Rates of HBV serological marker positivity stratified by sex, ethnicity, education, and residential area in 2010, 2013, and 2015

Variables	Sample tested (*n*)			HBsAg (%) (95% *CI*)			Anti-HBs (%) (95% *CI*)			Anti-HBc (%) (95% *CI*)		
	2010	2013	2015	2010	2013	2015	2010	2013	2015	2010	2013	2015
Sex												
Male	15,826	16,939	9,354	7.78 (6.51–9.03)	7.23 (6.12–7.59)	5.91 (5.27–6.43)[a]	24.42 (22.40–26.34)	52.78 (52.01–54.40)	53.82 (51.56–56.57)[b]	43.8 (39.98–47.79)	32.96 (31.25–34.67)	28.32 (26.03–29.87)[c]
Female	12,218	18,293	11,448	6.81 (5.92–7.59)	6.27 (5.43–6.88)	5.82 (5.28–6.13)	22.81 (20.49–25.23)	54.13 (52.61–55.66)	52.91 (50.68–54.61)[b]	43.9 (40.42–47.40)	32.78 (31.46–34.09)	26.17 (24.46–27.07)[c]
Ethnicity												
Han	26,515	33,611	19,068	7.31 (6.29–8.22)	6.63 (6.40–6.85)	5.91 (5.44–6.42)	23.52 (21.62–25.49)	54.53 (53.33–55.74)	53.47 (51.27–54.69)[b]	44.2 (40.58–47.82)	33.19 (31.78–34.60)	28.21 (26.65–29.93)[c]
Uighur	263	296	159	4.68 (3.82–5.61)	3.38 (2.71–4.05)	3.76 (0.78–6.77)	20.68 (19.03–22.42)	56.08 (49.29–62.87)	60.65 (53.34–67.68)[b]	43.1 (41.09–45.02)	15.65 (12.20–19.11)	19.64 (13.27–25.72)[c]
Tibetan	990	1,207	857	5.78 (4.50–7.09)	3.78 (2.25–5.30)	5.15 (3.75–6.74)	24.91 (16.58–33.28)	33.21 (29.50–36.92)	53.36 (51.50–56.18)[b]	24.5 (20.88–28.21)	24.46 (20.62–28.06)	26.13 (23.32–29.21)
Others	276	118	274	5.21 (2.89–7.51)	5.47 (2.42–8.64)	5.37 (2.76–8.18)	19.06 (6.82–31.29)	37.97 (18.62–57.33)	50.11 (49.18–59.03)[b]	31.5 (24.21–38.89)	23.58 (20.31–26.85)	22.36 (18.32–28.40)
Education (15–59 years)												
Illiterate and primary school	8,125	9,981	4,335	8.28 (6.81–9.78)	7.12 (6.78–7.54)	6.78 (6.43–7.36)	16.54 (14.72–18.40)	47.29 (45.32–49.04)	50.34 (49.01–52.03)[b]	43.21 (38.89–47.58)	37.55 (35.42–38.46)	36.24 (34.36–39.23)
Middle school	7,239	11,146	4,947	8.79 (7.26–10.28)	7.68 (7.21–8.32)	7.14 (6.49–7.84)	21.46 (19.51–23.46)	53.27 (50.24–55.36)	52.16 (51.57–54.35)[b]	45.38 (41.56–49.28)	35.42 (33.46–37.58)	29.27 (27.44–31.12)[c]
High school	3,397	3,521	1,671	8.21 (7.18–9.16)	6.65 (6.36–7.24)	5.41 (4.41–6.94)[a]	26.21 (22.78–29.68)	59.89 (57.64–62.56)	57.43 (55.02–59.76)[b]	43.78 (39.68–47.89)	26.86 (24.66–28.87)	26.49 (24.44–29.73)[c]
Junior college or undergraduate degree	1,294	1,566	1,735	5.79 (4.31–7.20)	3.83 (3.56–4.48)	3.17 (2.26–4.15)[a]	34.23 (30.21–38.18)	74.33 (69.62–76.32)	72.08 (70.05–74.27)[b]	42.32 (39.45–45.12)	20.24 (18.67–23.24)	22.75 (20.04–23.97)
Urban/rural												
Urban	6,092	8,768	5,221	6.12 (5.32–7.01)	5.04 (4.68–5.54)	4.83 (4.28–5.45)	24.02 (19.68–28.42)	57.14 (54.76–62.51)	55.18 (53.27–57.96)[b]	47.50 (45.71–49.28)	28.48 (26.34–32.42)	20.35 (18.72–21.83)[c]
Rural	21,952	26,464	15,137	7.72 (6.51–8.87)	6.60 (6.15–7.05)	6.04 (5.65–6.41)[a]	23.31 (21.53–25.02)	52.79 (51.88–53.70)	49.68 (48.33–51.93)[b]	42.28 (37.68–46.79)	34.29 (33.44–35.14)	30.26 (28.15–31.65)[c]

Note. *CI*, confidence interval; HBsAg, hepatitis B surface antigen; anti-HBs, antibody against hepatitis B surface antigen; anti-HBc, antibody against hepatitis B core antigen. [a]$P < 0.05$ for the comparison of the seropositive rate of HBsAg between 2010 and 2015. [b]$P < 0.05$ for the comparison of the seropositive rate of anti-HBs between 2010 and 2015. [c]$P < 0.05$ for the comparison of the seropositive rate of anti-HBc between 2010 and 2015.

male was higher than that in female; however, the difference was not statistically significant ($P > 0.05$). In addition, the *OR* values of the age groups above 14 and below 14 were 2.31, 2.18, and 2.43, respectively, indicating that people in higher age groups were more likely to be infected with HBV ($P < 0.05$). The possibility of HBV infection in ethnic minority group was slightly higher than that in the Han nationality group, but the difference was not statistically significant. The probability of HBV infection in rural population was significantly higher than that in urban population ($P < 0.05$) (See Supplementary Table S3 available in www.besjournal.com).

Decrease in the Incidence of Legally Reported HBV Infection

The incidence rates of legally reported HBV in Wuwei from 2010 to 2015 were 686.53/100,000, 659.37/100,000, 311.17/100,000, 87.16/100,000, 62.20/100,000, and 53.72/100,000, respectively. The average annual reported incidence of HBV exhibited a declining trend ($P < 0.05$) with an average decrease of 310.03/100,000. Nationwide, the statutory reported incidences of hepatitis B infection in China from 2010 to 2015 were 79.67/100,000, 81.73/100,000, 80.88/100,000, 71.29/100,000, 68.59/100,000, and 68.13/100,000, respectively. Compared with the overall statutory incidence of hepatitis B in China, Wuwei reported significantly higher incidence rates from 2010 to 2015 ($P < 0.05$; Figure 2).

DISCUSSION

Since its designation as a hepatitis B prevention and control demonstration area in 2009, Wuwei has implemented a series of prevention and control measures, including vaccination, health education, and physician training, with support from special funds and strong cooperation from local governmental departments. In this study, we investigated the prevalence of HBV serum markers in three representative populations in 2010, 2013, and 2015 in Wuwei. In general, the effects of the vaccine-based prevention and control measures implemented in 2010 became evident 5 years later. The HBsAg-positive rate in 2015 was 5.87% compared with the 7.19% recorded in 2010. The rate of anti-HBs positivity increased from 23.49% in 2010 to 53.72% in 2015 and was significantly higher in male and female participants, those of Han and Hui ethnicity, and urban and rural residents (all $P < 0.05$). Meanwhile, the incidence of statutory reports of HBV infection in Wuwei city decreased with each passing year from 2010 to 2015. By contrast, the rates of anti-HBc in these groups decreased significantly from 2010 to 2015 (all $P < 0.05$).

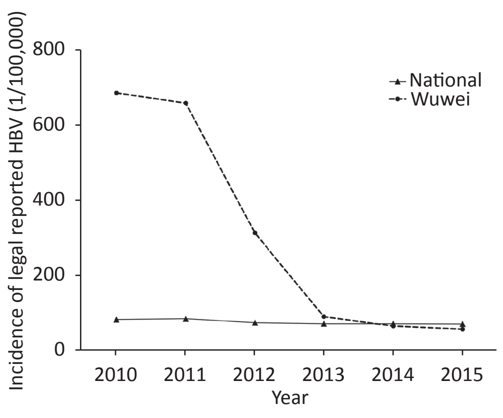

Figure 2. Incidence of HBV in Wuwei city according to national legal reports in 2010–2015.

Despite the above-listed improvements, 1.24% of children younger than 10 years in Wuwei were HBsAg-positive in 2015. This rate was significantly higher than that reported for the same age group (less than 1%) in a 2014 Chinese national serological survey[14], suggesting that measures intended to block the transmission of HBV from mother-to-child had not been fully achieved in Wuwei. A previous study investigated the risk factors for mother-to-child transmission of Hepatitis B among 221 HBsAg positive mothers who had delivered 247 infants in the obstetrics and gynecology departments of three Grade B hospitals in Wuwei city from 2008 to 2010[15]. The results showed that less than a third of premature and low-weight infants in Wuwei city had received the first dose of hepatitis B vaccine in time. The delayed injection of the first dose of HBV vaccine after premature birth was a possible risk factor for HBV mother-to-child transmission. Routinely, pregnant women with a high HBV load are administered with a blocking treatment that combines immunoglobulin with a HBV vaccine. However, this treatment fails to prevent HBV immunization in certain cases, which constitutes an important cause of vertical HBV transmission from mother-to-child in China[16-18]. The treatment of high viral load pregnant women infected with HBV with nucleotide analogs can reduce the level of HBV DNA in pregnant women, thus reducing the risk of mother-to-child transmission[19]. The high rate of infection observed among infants and young children in the 2015 survey may be attributable mainly to the fact that high-risk pregnant women in Wuwei had not received antiviral treatment during the survey period. Moreover, although the vaccination rate of hepatitis B vaccine for children under 5 years old in the study area was over 99%, the positive rate of anti-HBs was about 50%, which gradually decreased with the increase in age. Hence, the antibody titer of children should be monitored.

Compared with the results of the 2010 serosurvey, the rate of anti-HBs positivity increased significantly in 2013 and 2015. However, the prevalence of HBsAg in rural areas was higher than that reported by a national serological survey conducted during the same period[20]. This finding shows that the comprehensive prevention and control measures based on vaccination have achieved initial results in rural areas, but these findings need further confirmation. The three serosurveys also revealed that the rate of HBsAg positivity decreased, and that the rate of anti-HBs positivity increased as the education level increased. Given the generally lower level of educational attainment in the rural Chinese population, this factor may contribute to the lack of knowledge about hepatitis B prevention and immune awareness and consequently, to the high incidence of hepatitis B in this area. Therefore, strategies that target the rural villages of Western China should include a free vaccination policy to reduce the disease burden and the distribution of stronger propaganda intended to enhance the knowledge about hepatitis B prevention and treatment by community physicians serving village households. Furthermore, the positive rates of HBsAg and anti-HBc in 20–69-year-old adults remained high. Up to 20%–30% of adults with chronic HBV infection are estimated to develop cirrhosis or liver cancer[21]. The burden of hepatitis B-related diseases in Western China remains serious. At present, the main antiviral drugs for hepatitis B patients include nucleoside (acid) analogs and interferon. Hepatitis B patients treated with nucleoside analogs often need long-term use of drugs to inhibit HBV DNA replication in vivo and reduce the risk of cirrhosis and liver cancer[22,23]. New nuclear nucleoside drugs, and the development of sequential or joint treatment, such as Peg interferon, offer a new hope of ‘functional cure’ to hepatitis B patients[24,25]. However, given the economic backwardness of the region, the economic burden of antiviral treatment on patients cannot be ignored.

To eliminate hepatitis B by 2030 as proposed by the World Health Organization, we recommend the following improved strategies for hepatitis B prevention and control in Western China based on our findings: (1) implementation of antiviral drug intervention among HBsAg-positive pregnant women to block vertical HBV transmission; (2) strengthened monitoring of antibody titer in children in this region and implementation of a more comprehensive vaccination strategy; (3) strengthened publicity and education initiatives targeting the rural population, with rural physicians serving as mediators; (4) implementation of free adult vaccination strategies to reduce the economic burden associated with hepatitis B and related diseases. We also propose to establish and implement a comprehensive strategy for hepatitis B prevention and treatment that will integrate prevention, screening, diagnosis, and treatment throughout the human lifespan.

In summary, although vaccine-based prevention and control measures have achieved certain results in Wuwei area, the positive rate of HBsAg in children and rural population is still high, and the burden of hepatitis B remains heavy. We should further strengthen the prevention and control of rural population and children and the management of the infected to reduce the patient burden.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHORS’ CONTRIBUTIONS

Experiments conceived and designed by: YAN Yong Ping, GUO Zhi Wen, and SHAO Zhong Jun; Experiments carried out by: LIU Nan, JI Zhao Hua, GAO Jie, and LIU Yi Wen; Data analysis by: CHEN Hui, PU Zhong Shu, JI Zhao Hua, and YAN Yong Ping; Paper written by: CHEN Hui, JI Zhao Hua, and YAN Yong Ping.

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Supplementary Table S1. Population of different ages and genders in four districts and counties of Wuwei in 2010

Age (years)	Liangzhou		Gulang		Minqin		Tianzhu	
	Male	Female	Male	Female	Male	Female	Male	Female
0–	5,703	4,404	3,786	3,709	11,353	10,747	4,701	4,069
5–	27,786	21,787	5,760	6,238	14,840	14,046	4,802	4,162
10–	24,337	19,130	14,678	16,558	37,601	35,591	14,956	13,370
20–	68,771	62,692	18,150	18,891	34,927	33,058	12,555	12,519
30–	79,950	74,240	19,354	20,972	38,924	36,843	13,077	12,440
40–	88,510	83,790	28,461	29,618	27,451	25,983	20,050	18,926
50–	83,930	76,810	15,072	13,913	18,054	17,088	10,494	8,710
60–	80,500	77,710	13,783	16,384	12,590	11,917	6,928	7,258
70–	71,068	72,652	12,972	14,698	6,832	6,466	2,927	3,531
80–	3,317	3,627	7,379	10,492	1,974	1,868	514	606
Total	534,672	496,042	139,395	151,473	204,546	193,607	91,056	85,573

Supplementary Table S2. Total anti-HBs positive rate of 1–5-year-old children in 2013 and 2015 surveys

Age (years)	Investigation (*n*)	Anti-HBs		χ^2	*P*
		Positive	Positive rate (%)		
1	10	7	70.00		
2	39	28	71.79		
3	152	92	60.53	26.27	< 0.01
4	283	123	43.46		
5	356	153	42.98		

Supplementary Table S3. Multiple factor weighted logistic regression analysis of HBV infection in general population of Wuwei

Variables	2010				2013				2015			
	B	*SE*	*OR* (95% *CI*)	*P*	*B*	*SE*	*OR* (95% *CI*)	*P*	*B*	*SE*	*OR* (95% *CI*)	*P*
Sex												
Female			1.00				1.00				1.00	
Male	0.78	0.18	1.32 (1.21–1.44)	> 0.05	0.68	0.24	1.26 (1.01–1.44)	> 0.05	0.88	0.16	1.22 (1.09–1.35)	> 0.05
Age												
≤ 14			1.00				1.00				1.00	
> 14	1.88	0.04	2.31 (1.92–2.68)	< 0.05	1.68	0.06	2.18 (1.86–2.38)	< 0.05	1.48	0.05	2.43 (1.92-2.81)	< 0.05
Ethnicity												
Han			1.00				1.00				1.00	
Minorities	0.42	0.28	1.04 (1.02-1.14)	> 0.05	0.52	0.12	1.12 (1.06–1.27)	> 0.05	0.36	0.06	1.08 (1.02–1.15)	> 0.05
Education (15–59 years)												
Illiterate and primary school			1.00				1.00				1.00	
Middle school	0.59	0.04	1.02 (0.92–1.08)	> 0.05	0.47	0.06	0.92 (0.82–1.04)	> 0.05	0.46	0.04	0.94 (0.84–1.01)	> 0.05
High school	0.68	0.06	1.04 (0.84–1.12)	> 0.05	0.48	0.12	0.98 (0.89–1.12)	> 0.05	0.88	0.11	0.89 (0.74–0.96)	> 0.05
Junior college or undergraduate degree	0.76	0.12	0.64 (0.52–0.96)	< 0.05	0.86	0.22	0.74 (0.56–0.94)	< 0.05	0.56	0.12	0.63 (0.55–0.87)	< 0.05
Urban/rural												
Urban			1.00				1.00				1.00	
Rural	0.93	0.04	1.28 (1.14–1.36)	> 0.05	1.02	0.03	1.24 (1.16–1.35)	> 0.05	1.01	0.05	1.31 (1.14–1.42)	> 0.05

Note. *B*: regression coefficient; *SE*: standard error; *OR*: odds ratio