Change of the prevalence of hepatitis B and its related factors in Inner Mongolia between 2006 and 2020

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Abstract

Background: The course of hepatitis B is prolonged and easy to turn into chronic hepatitis, cirrhosis and liver cancer as the second serious disease-causing human cancer.Hepatitis B not only affects the health of individuals, but also causes a heavy economic burden to the family society.In 2015, WHO launched a strategy to eliminate hepatitis as a public health threat by 2030; however, annual global deaths from HBV are projected to increase by 39% between 2015 and 2030 if the status quo is maintaine.Mortality from HBV-related liver diseases in China with the highest burden of HBV infection accounts for 30% of the global mortality from HBV infection. It’s important for China to achieve the WHO goal of global hepatitis eradication by 2030.In the past three decades, China has made timely vaccination of newborns and infants a top priority to prevent and control hepatitis B.The infection rate of HBV has decreased significantly, and our country is no longer a high-prevalence area.However, large differences in the burden of hepatitis B virus exist not only between countries and regions, but also within a country or region, varying by state or province, income, race or ethnicity, and other social and cultural factors. Inner Mongolia located in the north of China and life style has greater specificity. HBV vaccination has been carried out in Inner Mongolia for many years. However, few studies have been conducted to evaluate the actual effects of the vaccine after using.

Objective: To compare the prevalence rate of hepatitis B virus serum markers in Inner Mongolia between 2020 and 2006, and understand the change of hepatitis B prevalence in the past 15 years, and provide scientific basis for the development of hepatitis B prevention and control plan.

Methods: A stratified multi-stage cluster random sampling method was adopted in 12 areas of Inner Mongolia. The subjects

aged 1-60 years old were selected to carry out questionnaire survey and sample collection and detect hepatitis B serum biomarkers, including HBV surface antigen (HBsAg), HBV surface antibody (HBsAb) and HBV core antibody (HBcAb). The prevalence of serum biomarkers of hepatitis B was analyzed and compared between 2020 and 2006 which were standardized by age and sex.

Results: There were 6,500 subjects in 2020 and 6304 subjects in 2006. HBV infection rate was 22.69% (95%CI 21.67%-23.71%) and 30.06% after standardization. The positive rate of HBsAg was 2.06%, lower than 2.74% in 2006 (P=.012) with the decrease proportion of 24.82%. After the standardization using the population in the Inner Mongolia by age and sex, the prevalence of HBsAg was also lower in 2020 than in 2006 (2.75% vs. 4.11%, P<.001). Men and the subjects without the HBV vaccination were related with HBsAg prevalence. The same results were observed in the serum biomarker of HBsAb (44.65% vs. 47.76%, P<.001; standardized 41.40% vs. 42.14%, P=.39) and HBcAb (14.63% vs. 16.24%, P=.012; standardized 20.15% vs. 22.91%, P<.001).

Conclusions: The burden of HBV infection in Inner Mongolia has decreased significantly. The prevention and control of hepatitis B in Inner Mongolia should continue to strengthen, not only pay more attention to hepatitis B vaccination, but also emphasize the active treatment after HBV infection.

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Change of the prevalence of hepatitis B and its related factors in Inner Mongolia between 2006 and 2020

ABSTRACT

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Conclusions: The burden of HBV infection in Inner Mongolia has decreased significantly. The prevention and control of hepatitis B in Inner Mongolia should continue to strengthen, not only pay more attention to hepatitis B vaccination, but also emphasize the active treatment after HBV infection.

Keywords: Hepatitis B; cross-sectional study; HBV prevalence; related factors

Introduction

The course of hepatitis B is prolonged and easy to turn into chronic hepatitis, cirrhosis and liver cancer as the second serious disease-causing human cancer[1]. Hepatitis B not only affects the health of individuals, but also causes a heavy economic burden to the family

society. The world health organization (WHO) reported data showed that the global lived about 257 million cases of chronic HBV infection, every year 87000 people died when the hepatitis B related disease in 2015[2-4]. Studies have shown that the prevalence of hepatitis B varies by geographic region, ranging from low prevalence areas in the United States and Western Europe (0.1%-2%), to moderate prevalence areas in Mediterranean countries and Japan (2%-8%), to high prevalence areas in sub-Saharan Africa (8%-20%). HBV is more prevalent in Africa and many Asia-Pacific regions[5, 6]. Differences in prevalence among countries are mainly due to differences in routine hepatitis B vaccination policies between countries, which in turn affect immunity, and gaps in hepatitis B vaccination among health care workers despite WHO vaccination recommendations and national immunization guidelines. In 2015, WHO launched a strategy to eliminate hepatitis as a public health threat by 2030; however, annual global deaths from HBV are projected to increase by 39% between 2015 and 2030 if the status quo is maintained[7]. Mortality from HBV-related liver diseases in China with the highest burden of HBV infection accounts for 30% of the global mortality from HBV infection. It’s important for China to achieve the WHO goal of global hepatitis eradication by 2030[8].

In the past three decades, China has made timely vaccination of newborns and infants a top priority to prevent and control hepatitis B[9]. In 2002, China included hepatitis B vaccine in the Expanded Program on Immunization (EPI), providing free vaccination for children under 14 years of age[10]. In addition, in 2009-2011, a catch-up campaign targeting children under 15 years of age was launched, successfully vaccinating about 6.8 million children[11]. These measures significantly reduced the prevalence of HBsAg in the Chinese population from 9.8% in 2000 to 7.2% in 2006 with the prevalence of HBsAg in children under 10 years old to 1.5% in 2006 and under one year old to 0.69%[10]. HBsAb were detected in 60% of children under 13 years of age[8]. The infection rate of HBV has decreased significantly, and

our country is no longer a high-prevalence area[12, 13].

However, large differences in the burden of hepatitis B virus exist not only between countries and regions, but also within a country or region, varying by state or province, income, race or ethnicity, and other social and cultural factors[7]. Inner Mongolia located in the north of China and life style has greater specificity. HBV vaccination has been carried out in Inner Mongolia for many years. However, few studies have been conducted to evaluate the actual effects of the vaccine after using.

This study analyzed the prevalence of three hepatitis B serologic results of HBsAg, HBsAb and HBcAb in 2020 compared to the 2006 to demonstrate the changes in local risk factors for hepatitis B virus infection and provide the intervention measures and achieve the goal of eliminating HBV by 2030.

Methods

Subjects

According to the requirements of the national viral hepatitis immune evaluation survey in 2020, the multi-stage stratified random sampling method was used to select subjects aged 1-60 years old from 12 urban areas in Inner Mongolia. According to the Statistical Yearbook of Inner Mongolia (2019) and the regional nature of each banner county, the sampled banner counties were divided into urban, rural and pastoral areas, and two neighborhood committees were randomly selected from each of the regions. The latest permanent subject's information of the selected regions was recorded and stratified random sampling was conducted. First, each resident is assigned a unique code based on their region. Secondly, the residents are divided into four age groups, namely 1-4 years old, 5-14 years old, 15-29 years old and 30-60 years old. Third, the random sampling was conducted within each age group, and the sample size was expanded to 926, 1297, 1367, 2910, for a total of 6500. Finally, the survey should be

carried out according to the resident list, and 1802 specimens were collected in urban areas, 2069 specimens in rural areas, and 2629 specimens in pastoral areas until the required sample size of the four age groups was completed.

Information collecting

The questionnaire were collected and filled out by professionally trained personnel. The contents of the questionnaire included general demographic characteristics (gender, age, occupation, etc.), hepatitis history and hepatitis B vaccination history based on the vaccination certificate.

Sample collection and laboratory detection

Venous blood was collected and serum was separated naturally and frozen at -20℃ for examination. The Inner Mongolia Center for Disease Control and Prevention used Abbott chemiluminescent particle immunoassay to detect three serological indicators of HBsAg, HBsAb and HBcAb. The test kit includes HBsAg Reagent Ki (REF:08P0874 LOT:4548FN01), Anti-HBs Reagent Ki (REF:07P8974 LOT:4831FN01), Anti-HBc II Reagent Ki (REF:07P8774 LOT:46038BE01) by Abbott automatic chemiluminescence immunoanalyzer (Model: Alinity i). All the tests were performed according to the kit instructions. About the standard of hepatitis B virus surface antigen detection, samples with a concentration <0.5 IU/mL were considered non-reactive, and samples with a concentration ≥0.5 IU/mL were considered reactive. For the same reason of hepatitis B virus surface antibody, samples with a concentration <10 mIU/mL were considered non-reactive, and samples with a concentration ≥10 mIU/mL were considered reactive. For the hepatitis B virus core antibody, samples with concentrations <1.0 S/CO were considered non-reactive, and samples with concentrations ≥1.0 S/CO were considered reactive.

Statistical analysis

We used Excel for data collection and STATA software (Version 17.0) was used to collate

the survey data, calculate the positive rate of HBV markers, and multivariate analysis was used to determine the factors related to the positive rate of HBsAg and HBsAb and HBcAb. A precise method based on binomial distribution was used to calculate the corresponding 95% confidence interval (CI), where the difference between groups was compared by χ^2 test at the level of $\alpha=0.05$. Multiple logistic regression model was used to further study the potential factors affecting HBV infection.

Ethical considerations

This study was approved by the Ethics Committee of Inner Mongolia CDC and conducted in accordance with the national ethical code. The survey was conducted in accordance with the ethical guidelines of the Declaration of Helsinki. Participants were informed of the purpose of the survey, and informed consent was provided before samples were collected. Their data will be kept confidential.

Results

Basic information

A total of 6500 subjects aged 1-60 years were included in 2020, of which 2972 (45.72%) were male in Table 1. The nation of Han accounted for 453 (68.51%); Urban, rural and pastoral areas accounted for 27.72%, 31.83% and 40.45% respectively. The subjects aged 18-44 years made up the largest proportion accounted for 38.65%. A total of 6304 subjects aged 1-60 years were investigated in 2006. The basic information of subjects were comparable because of their little proportion differences between 2006 and 2020, although the statistical significance was observed.

All the subjects aged 1-14 years have completed hepatitis B vaccination. From the perspective of vaccination time, 97.43% subjects got the first dose of hepatitis B vaccination within 24h after born, higher than 80.57% in 2006 (P<.001); 96.97% subjects finished three

dose of hepatitis B vaccination, higher than 89.35% in 2006 (P<.001). The rates of one-dose injection timely and three-dose injection were higher in urban areas than in rural or pastoral areas (P<.001) in Table 2 and Table 3. The rates of one-dose injection timely was 99.68% (95%CI 98.99%-99.90%) and three-dose injections was 99.46% (95%CI 98.71%-99.78%) under 5 years, higher than in other ages (P<.001)

Table 1. The basic information of subjects in Inner Mongolia in 2020 and 2006

Characteristics	2020		2006		
	No.	Proportion (%)	No.	Proportion (%)	P
Sex					.37
Male	2972	45.72	2932	46.51	
Female	3528	54.28	3372	53.49	
Nation					<.001
Han	4453	68.51	4173	66.20	
Mongol	1863	28.66	1539	24.41	
Other	184	2.83	592	9.39	
Age, years					<.001
≤4	926	14.25	795	12.61	
5-17	1569	24.14	2463	39.07	
18-44	2512	38.65	2315	36.72	
45-60	1493	22.97	731	11.60	
Region					<.001
Urban	1802	27.72	2352	37.31	
Rural	2069	31.83	1942	30.81	
Pastoral	2629	40.45	2010	31.88	
Education level					<.001
Primary	655	15.31	511	14.73	
Junior	1175	27.47	1441	41.55	
Senior	974	22.77	874	25.21	
College	1473	34.44	642	18.51	
Occupation					<.001
Student	347	28.63	949	27.36	
Peasant-worker	1212	28.34	741	21.37	
Teacher/Office	765	17.89	441	12.72	
Healthcare workers	257	6.01	144	4.15	

Other	1696	39.65	1193	34.40

Table 2 The status about one-dose of hepatitis B vaccination within 24h after born in aged 1-14 years in 2020 and 2006 in Inner Mongolia

Characteristics	2020			2006			P
	No.	Rate (%)	95% CI	No.	Rate (%)	95% CI	
Sex							
Male	1106	97.53	96.45-98.29	1144	79.5	77.33-81.51	<.001
Female	1015	97.31	96.14-98.14	1141	81.67	79.56-83.62	<.001
Age, years							
≤4	923	99.68	98.99-99.90	701	88.18	85.74-90.25	<.001
5-10	806	98.77	97.74-99.35	1081	84.45	82.36-86.34	<.001
11-14	392	90.11	86.92-92.59	503	66.1	62.65-69.38	<.001
Nation							
Han	1422	97.20	96.21-97.93	1492	80.13	78.25-81.88	<.001
Mongol	647	98.03	96.63-98.85	536	76.24	72.95-79.25	<.001
Other	52	96.30	85.97-99.10	257	94.83	91.45-96.92	.65
Region							
Urban	683	99.71	99.30-100.11	1014	94.94	93.63-96.26	<.001
Rural	725	94.52	92.91-96.13	669	72.25	69.36-75.14	<.001
Pastoral	713	98.34	97.41-99.28	602	71.50	68.44-74.55	<.001

Table 3 The status about three-dose hepatitis B vaccination in aged 1-14 years in 2020 and 2006 in Inner Mongolia

Characteristics	2020			2006			P
	No.	Rate (%)	95% CI	No.	Rate (%)	95% CI	
Sex							
Male	1100	97.00	95.83-97.85	1273	88.46	86.71-90.02	<.001
Female	1011	96.93	95.69-97.82	1261	90.26	88.59-91.71	<.001
Age, years							
≤4	921	99.46	98.71-99.78	770	96.86	95.38-97.87	<.001
5-10	799	97.92	96.67-98.70	1202	93.91	92.45-95.09	<.001
11-14	391	89.89	86.67-92.39	562	73.85	70.60-76.85	<.001
Nation							
Han	1413	96.58	95.52-97.40	1648	88.51	86.98-89.88	<.001
Mongol	646	97.88	96.45-98.74	621	88.34	85.74-90.51	<.001
Other	52	96.29	85.97-99.10	265	97.79	95.14-99.01	.52
Region							
Urban	676	98.69	97.83-99.54	1025	95.97	94.79-97.15	<.001
Rural	722	94.13	92.91-96.14	800	86.39	84.18-88.61	<.001
Pastoral	712	98.21	97.24-99.18	709	84.20	65.01-70.68	<.001

HBV infection

HBV infection rate was 22.69% (95%CI 21.67%-23.71%) and 30.06% after standardization in 2020. Compared with 2006, the HBV infection rate in each region of Inner Mongolia was lower in Figure 1 and in Figure 2. The possible factors related to HBV infection were male (OR=1.173, 95%CI 1.023-1.345) and age (OR=1.602, 95%CI 1.339-1.917), and the patients who didn't accept hepatitis B vaccine (OR=3.837, 95%CI 3.188-4.617) in 2020. Other than the above factors, student subjects (student *vs.* Teacher, OR=1.734, 95%CI 1.290-2.330; student *vs.* healthcare workers, OR=1.838, 95%CI 1.073-3.147) and low education level (primary *vs.* Junior, OR=1.734, 95%CI 1.290-2.330; primary *vs.* Senior, OR=1.838, 95%CI 1.073-3.147) were also related with HBV infection in 2006.

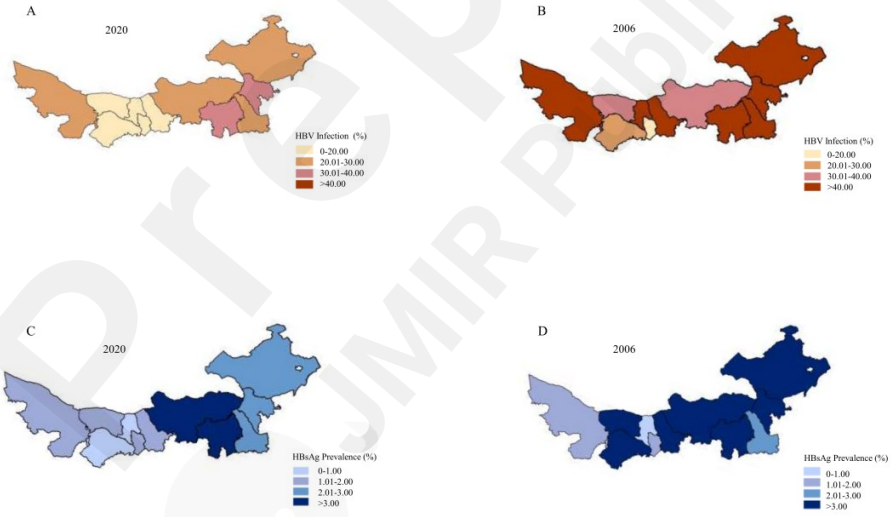

Figure. 1 The infection rate of HBV and the prevalence rate of HBsAg in each region of Inner Mongolia in 2020 and 2006. **a** The infection rate of HBV in each region of Inner Mongolia in 2020. **b** The infection rate of HBV in each region of Inner Mongolia in 2006. **c** The prevalence rate of HBsAg in each region of Inner Mongolia in 2020. **d** The prevalence rate of HBsAg in each region of Inner Mongolia in 2006.

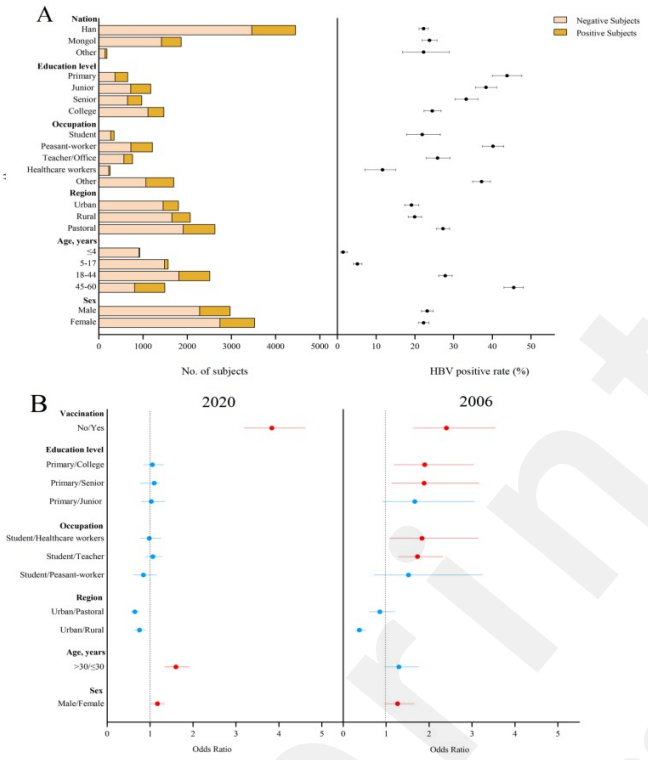

Figure. 2 The infection rate of HBV in different subjects in 2020 and possible factors related to HBV infection in 2020 and 2006 of Inner Mongolia. **a** The positive result and 95% CI for positive rate of HBV in different subjects of Inner Mongolia in 2020. **b** The possible factors related to HBV infection in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.

Prevalence of HBsAg

The positive rate of HBsAg was 2.06% (95%CI 1.72%-2.41%) in 2020 and 2.74% (95%CI 2.34%-3.15%) in 2006 (P=.012; standardized 2.75% *vs.* 4.11%, P<.001) in Figure 3. The positive rate of HBsAg was 2.29% (95%CI 1.81%-2.89%) in males and 1.87% (95%CI 1.47%-2.37%) in females (P=.24; standardized 1.18% *vs.* 0.90%, P=.28). The subjects with the nationality of Mongolia had a higher HBsAg positive rate of 2.63% (95%CI 1.99%-3.46%) than 1.86% (95%CI 1.51%-2.31%) with Han nationality (P=.095). The positive rate of HBsAg in urban areas was 0.89% (95%CI 0.54%-1.44%), which was significantly lower than those in rural and pastoral areas (1.69% and 3.16%, both P<.001). Among the different age groups, the lowest positive rate of HBsAg was 0.11% (95%CI 0.02%-0.76%) in children aged under 5 years. Among the subjects aged 15-60

years, the positive rate of HBsAg was inversely proportional to the level of education. The highest positive rate of HBsAg was 6.11% (95%CI 4.51%-8.22%) in the subjects with primary school education or below, and 3.88% (95%CI 2.92%-5.12%) in farmers. The possible factors related to the prevalence of HBsAg were male (OR=1.310, 95%CI 0.927-1.864) and hepatitis B vaccination history (OR=1.844, 95%CI 1.069-3.181) in 2020. However, hepatitis B vaccination history was not associated with the risk of the prevalence of HBsAg in 2006.

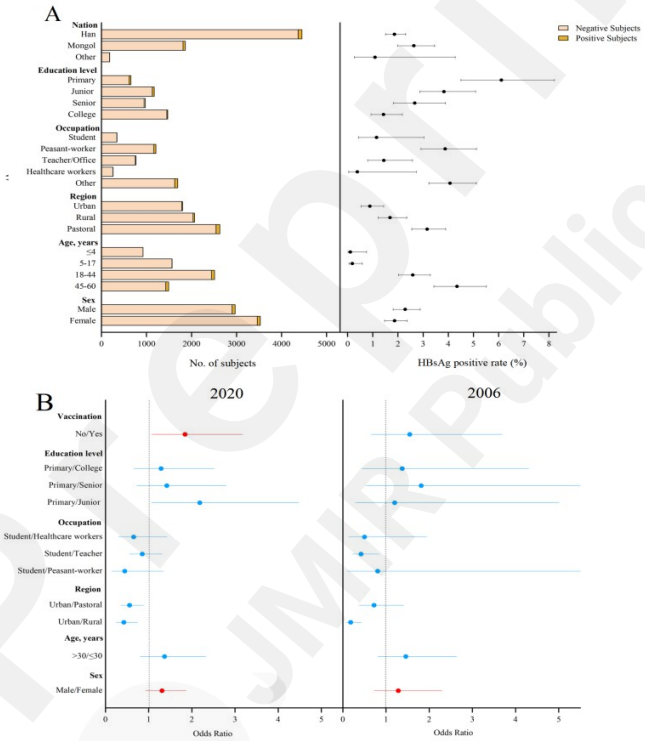

Figure. 3 The prevalence of HBsAg in different subjects in 2020 and the possible factors related to prevalence of HBsAg in 2020 and 2006 of Inner Mongolia. **a** The positive result and 95% CI for positive rate of HBsAg in different subjects of Inner Mongolia in 2020. **b** The possible factors related to HBsAg prevalence in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.

Prevalence of HBsAb

The prevalence of HBsAb in the subjects aged 1-60 years was 44.65% in 2020 and 44.76% in 2006 (P<.001) in Figure 4. There were 41.40% and 42.14% (P=.39) after standardized by age and sex using the whole Inner Mongolia population. The highest positive rate of HBsAb was 69.98% (95%CI 66.94%-72.85%) in children under 5 years, while the lowest positive rate of HBsAb was 36.52% (95%CI 34.17%-38.94%) aged 5-17 years. The rural area had the lowest positive rate of HBsAb (41.61%, 95%CI 39.51%-43.75%, P=.002) compared to other two regions. The positive rate of HBsAb was the highest among healthcare workers (62.26%, 95%CI 56.15%-68.00%) and the lowest among students (34.58%, 95%CI 29.75%-39.76%). The occupation (student *vs.* healthcare workers, OR=1.252, 95%CI 1.053-1.489) and hepatitis B vaccination history (OR=2.064, 95%CI 1.774-2.401) were related to the positive rate of HBsAb.

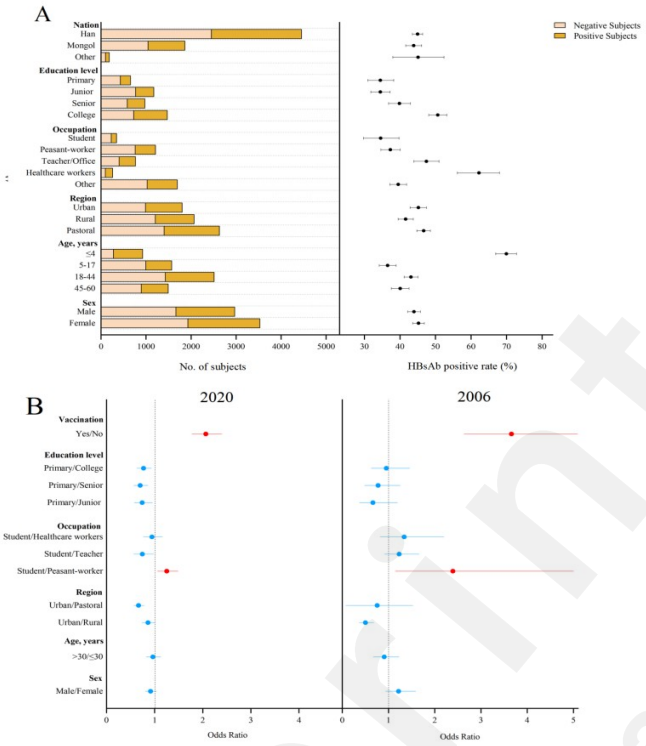

Figure. 4 The positive rate of HBsAb in different subjects in 2020 and the possible factors related to HBsAb positive in 2020 and 2006 of Inner Mongolia. **a** The positive result and 95% CI for positive rate of HBsAb in different subjects of Inner Mongolia in 2020. **b** The possible factors related to HBsAb positive in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.

Prevalence of HBcAb

The positive rate of HBcAb in the aged 1-60 years was 14.63% (95%CI 13.77%-15.49%) in 2020 which was lower than 2006 (P=.012; standardized 20.15% *vs.* 22.91%, P<.001) in Figure 5. The positive rate of HBcAb was 1.40% (95%CI 0.82%-2.40%) under 5 years old. The patients in the urban area had the lowest positive rate of HBcAb was 9.66% (95%CI 8.37%-11.11%). The positive rate of HBcAb in students was 4.32% (95%CI 2.62%-7.06%) and the positive rate of HBcAb in the subjects with college education was 11.0% (95%CI 9.50%-12.70%). The possible factors related to the positive rate of HBcAb were male (OR=1.298, 95%CI 1.110-1.518) and age (OR=3.246, 95%CI 2.541-4.146), and the lowest education level (primary *vs.* junior,

OR=2.387, 95%CI 1.736-3.282; primary *vs.* senior, OR=2.140, 95%CI 1.601-2.848; primary *vs.* College, OR=2.044, 95%CI 1.558-2.680). Compared with 2006, occupation was not associated with the positive rate of HBcAb.

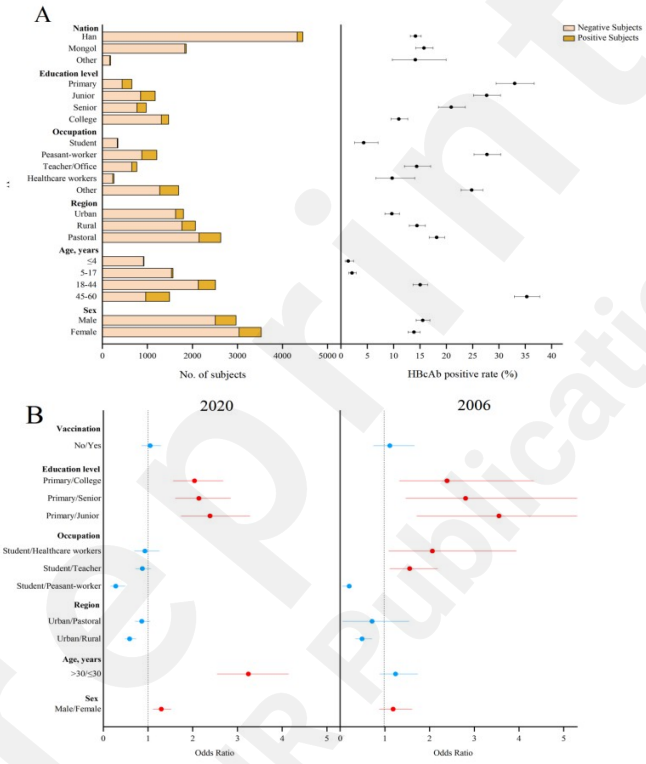

Figure. 5 The positive rate of HBcAb in different subjects in 2020 and the possible factors related to HBcAb positive in 2020 and 2006 of Inner Mongolia. **a** The positive result and 95% CI for positive rate of HBcAb in different subjects of Inner Mongolia in 2020. **b** The possible factors related to HBcAb positive in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.

Discussion

Chronic hepatitis B is a major global health challenge, with mortality rates from human immunodeficiency virus (HIV) infection, malaria and tuberculosis continuing to decline over the past 20 years, but deaths from viral hepatitis are still increasing[14]. Existing drugs can reduce the risk of progression of liver disease, but cannot absolutely eradicate HBV, therefore, prevention of HBV

infection remains the most effective strategy for controlling viral hepatitis B[15].

Various prevention and control measures have been introduced to control the epidemic of hepatitis B in Inner Mongolia. In 2002, Inner Mongolia officially included hepatitis B vaccination for newborns into the planned immunization of children, and the first dose of hepatitis B vaccine was given to newborns in a timely manner according to the principle of "who delivers the baby, who gets the vaccine" and the requirements of the hepatitis B vaccine immunization procedure. In 2013, the GAVI Project (GAVI/Children's Vaccine Fund cooperation project) was launched. The hepatitis B vaccination rate in the city as a unit reached more than 80% by the end of 2005, and the timely vaccination rate of the first injection reached more than 65%. According to the results of the hepatitis B survey in the whole population of the district in 2006, the established goals of the project were completed. In 2007, the Inner Mongolia Department of Health listed hepatitis B as one of the major infectious diseases, clearly proposed that the autonomous region finance provide subsidy funds, formulated and issued the 2007-2010 Inner Mongolia Viral Hepatitis Prevention and Control Plan, and proposed the control of hepatitis B indicators: the hepatitis B surface antigen carrying rate of children under 10 years old to reduce to less than 1%; The hepatitis B surface antigen carrying rate of the whole population has been reduced to less than 6%, the hepatitis B vaccine immunization rate of newborns has reached more than 85%, and the timely vaccination rate of the first injection has reached more than 75%. The implementation plan of the hepatitis B vaccine project issued by the Inner Mongolia Department of Health in 2011 determined that the children born

between 1996 and 1997 who had not received or had not completed three doses of hepatitis B vaccine should be vaccinated and revaccinated. In 2012, in order to control mother-to-child transmission of hepatitis B, in some areas of Inner Mongolia, the prevention of mother-to-child transmission of hepatitis B was listed as a major public health service project and a livelihood project of the government, which was jointly implemented by health and family planning. All women of childbearing age who planned to become pregnant and pregnant women were included in standardized management, and continuous services of free screening, detection, prevention and follow-up were implemented. Under the implementation of these series of policies, on the one side, we successfully participated in the research on the blocking technology of mother-to-child transmission of hepatitis B and reduced the chance of mother-to-child transmission . On the other side, the hepatitis B vaccination coverage in Inner Mongolia has been greatly improved.

The burden of hepatitis B infection decreased in Inner Mongolia in 2020

The prevalence rate of HBV surface antigen in children under 5 years of age in Inner Mongolia in 2020 was 0.1%, which reached the target of controlling prevalence of HBsAg in children under 5 years of age below 1% as mentioned in China Viral Hepatitis Prevention and Control Program (2017-2020). The analysis of factors related to HBV infection was conducted on the results of two surveys in 2006 and 2020 years, and the results showed that age (>30 years old) was a risk factor for HBV infection, and age was inversely proportional to the positive rate of HBsAg, considering that the increase in the prevalence of HBsAg at a specific age was more likely to be related to the legacy of infection occurring in early life[16]. The male population is a risk factor for HBV

infection. Studies have reported that in all geographical regions, the prevalence of chronic HBV in males was higher than that in females, and the incidence, prevalence and mortality of hepatocellular carcinoma (HCC) in males are also higher than that in females[17]. The risk of HCC in males is 2 to 3 times that of females[6, 18]. The data study results of 2006 showed that people with primary school education and below and students with occupation were the risk factors related to HBV infection, which was consistent with the research results at that time. The data of 2020 years showed that although the differences in the prevalence of HBsAg among groups with different educational experience and occupation were statistically significant, from the overall analysis.

Nearly all patients with persistent or cured HBV infection are seropositivity for HBcAb, an antibody that appears early in infection and is mostly present throughout life[19]. The factors of influencing of positive of HBcAb may be related to the lack of timely vaccination in early life or close contact within the family[20]. The results of this study also prove that the age group over 30 years old was one of the risk factors for the positive rate of HBcAb. Considering that the hepatitis B vaccine was included in the immunization program in 1992 and the accessibility or coverage was not perfect at the beginning of its introduction, this group of subjects was likely to have been infected in the past[21]. Studies have shown that the positive of HBcAb is an independent prognostic factor for HBV-associated primary liver cancer patients regardless of whether they receive hepatitis B vaccine[19]. So early antiviral treatment and health education should be provided to these subjects to prevent them from developing chronic hepatitis B, cirrhosis or liver cancer.

The important role of vaccination in hepatitis B prevention and control

Hepatitis B vaccination has had a well-documented positive impact on the global prevalence of hepatitis B infection, currently affecting an estimated 2.51 million people worldwide, and has reduced the prevalence of HBsAg among children under 5 years of age in the immunized child population to less than 2%, with estimates that by 2030, Hepatitis B vaccination in infants and newborns alone could prevent 2.11 million deaths[22-25].

The effect of HBV vaccine immunization in Inner Mongolia was remarkable, and the results of two investigations both proved that hepatitis B vaccination was a protective factor for HBV infection. The rate of the one-dose Hep-B vaccination in newborn within 24h of birth in China was 95%, and the rate of the three-dose hepatitis B vaccination was 99% in 2019[9]. The rate of the one-dose hepatitis B vaccination for children aged 1-14 years in Inner Mongolia reached the national average vaccination level, and the rate of the three-dose Hep-B vaccination was lower than the national average vaccination level in 2020. The rate of the one-dose and three-dose hepatitis B vaccination in urban areas are higher than those in rural and pastoral areas, which may be related to incomplete vaccination due to the inconvenient communication and transportation in some rural and pastoral areas and the loss of follow-up[26]. The rate of the one-dose and three-dose hepatitis B vaccination in 11-14 years were lower than the rate under 10 years old. This proved that the planned immunization policy in Inner Mongolia was effective and we should stick. There is little reason to stop or delay hepatitis B vaccination, and the delay or abandonment of vaccination is often due to the misjudgment of the vaccine contraindications. Minor diseases, family history of convulsions, general

allergies, antibiotic treatment, premature birth or low birth weight infants, human immunodeficiency virus infection, and postnatal jaundice are not contraindication, but a survey showed that these reasons accounted for 47.1% of the reasons for one-dose hepatitis B vaccination failure in Inner Mongolia. It is very important for each vaccination unit to accurately grasp the contraindications of vaccination and further improve the timely vaccination rate of newborn hepatitis B vaccine and the full vaccination rate of children.

The persistence of HBsAb and the ability of the immune system to respond to HBV exposure later in life are necessary for long-term prevention of HBV infection[27]. When hepatitis B vaccine was administered at birth that can avoid infection approximately 90%[11]. This study showed that the positive rate of HBsAb was statistically significant among different age groups, with the highest positive rate of HBsAb in the age group below 5 years old and the lowest positive rate of HBsAb in the age group 5-17 years old. This may be due to the natural attenuation of the antibody level after Hepatitis B immunization, which gradually decreases or disappears over time[27-29]. While the age group above 17 years old was more likely to naturally acquire hepatitis B immunity through previous infection. The HBsAg positive rate and HBV infection rate of children born to HBsAg positive and negative/unknown mothers were not statistically significant, indicating that Inner Mongolia has adhered to the comprehensive prevention and control strategy based on neonatal Hep-B vaccination since 2002, and adopted combined immunization measures (Hep-B combined immunoglobulin) for newborns born to HBsAg positive mothers. It has achieved remarkable results and effectively protects newborns from HBV infection. The new version of the National Immunization Program Vaccine

Immunization Procedures and Instructions for Children (2021) stipulates that newborn born to hepatitis B surface antigen positive mothers should receive hepatitis B vaccine within 12 hours after birth, and at the same time, 10 international units of hepatitis B immunoglobulin (HBIG) can be injected intramuscular in different parts (limbs) according to the doctor's advice. Higher requirements have been put in place for newborns born to positive mothers to be vaccinated against hepatitis B in a timely manner, further reducing the chance of mother-to-child transmission.

Limitations of this study

First of all, the laboratory detection methods used in the two experiments were different. Enzyme-linked immunosorbent assay (ELISA) was used in 2006, and Abbot chemiluminescence microparticle immunoassay (CMIA) was used in this experiment. Chemiluminescence method was used to determine the luminescence intensity through the instrument to determine the content of the substance to be measured, while enzyme-linked immunosorbent method was used to carry out semi-quantitative detection through a certain reaction between the substrate and the enzyme. Different experimental methods may lead to errors in the results of the two experiments. However, relevant studies have proved that the sensitivity and specificity of the two detection techniques for HBV were high[30, 31]. Secondly, in this study, we mainly used HBsAg seroprevalence as the primary marker of HBV infection, while other biomarkers such as HBV e antigen, antibodies, or DNA viral load were not detected, limiting the accuracy of testing the infection status of individuals, especially those with latent infection.

Conclusions

Compared with 2006, the positive rate of HBsAg and the infection rate of HBV all had decreased in Inner Mongolia in 2020. The positive rate of HBsAg in Inner Mongolia was different indifferent subjects in age, region and occupation. The positive rate of HBsAb covered by immunization program was not high, but the positive rate of HBsAg was low. It suggested that we should further do a good job of hepatitis B vaccination, supervise the one-dose injection timely for newborns and three-dose vaccination for children, and strengthen the hepatitis B vaccination for adults. We can popularize the knowledge of HBV prevention and treatment in key areas (rural and pastoral areas) and key groups (low education level, farmers, workers). Continue work should be performed to further reduce the burden of HBV morbidity and mortality towards the global goal of eliminating HBV.

Declarations

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Competing interests: The authors declare that no competing interests exist.

Ethics approval and consent to participate: Written informed consent for the use of their clinical samples was obtained from all individuals included in the study or from their guardians. The study was approved by the Ethics Review Committee of the Inner Mongolia Center for Disease Control and Prevention; all experimental protocols were approved by the Ethics Review Committee; and the methods were carried out in accordance with the approved guidelines.

Author contribution: QL, XT, ZZ conceived and designed the experiments; XR, FH, XW, CL, LW, JM, LZ, YW, SW, CG, SW and JG were in charge of sample collection; XD, SD and CL performed the experiments; XD, YZ and HS analyzed the data; XD and ZZ wrote the main manuscript and prepared all the tables and figures; and all authors reviewed the manuscript. All authors read and approved the final manuscript.

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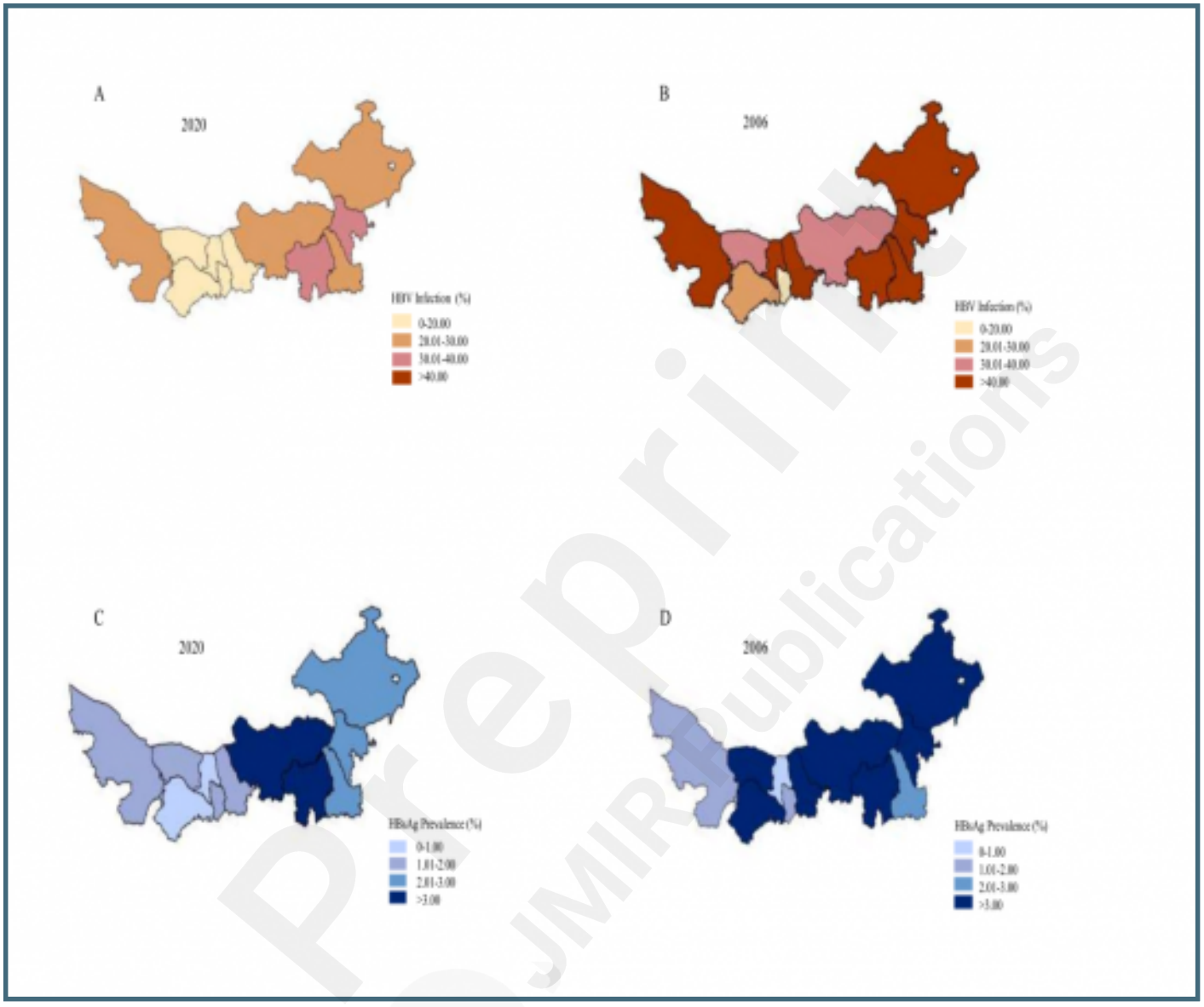
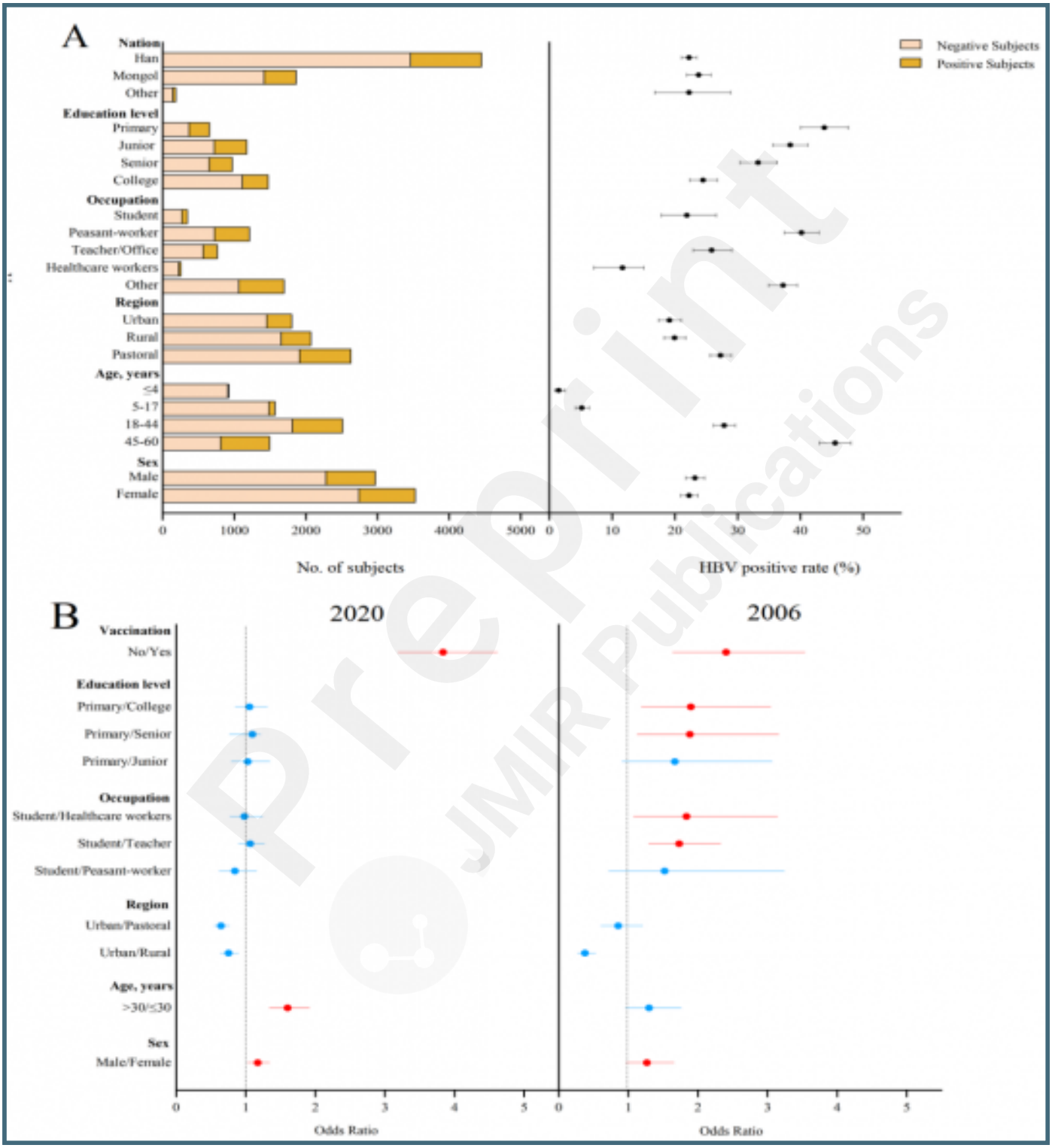
Supplementary Files

Figures

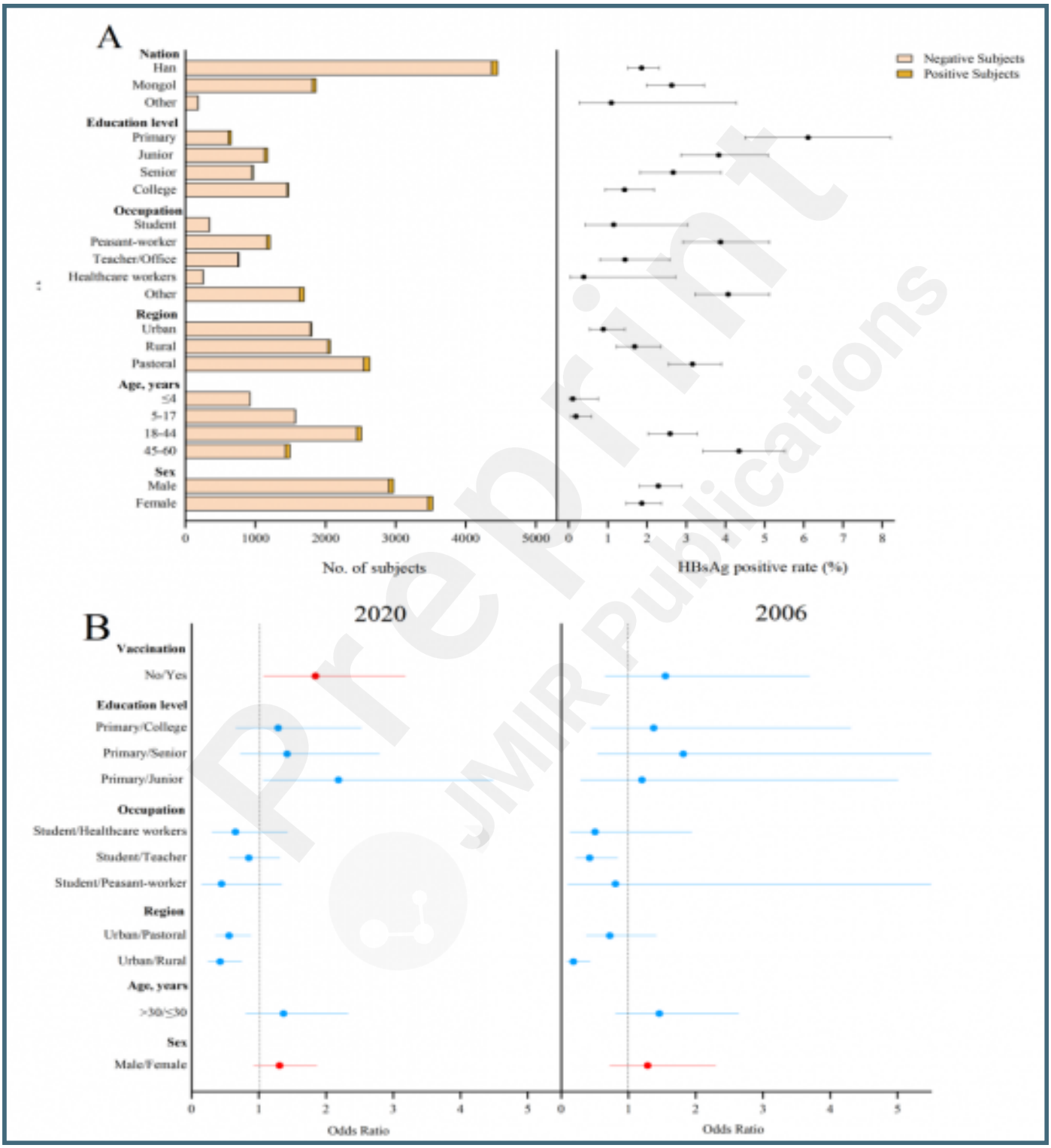
The infection rate of HBV and the prevalence rate of HBsAg in each region of Inner Mongolia in 2020 and 2006. a The infection rate of HBV in each region of Inner Mongolia in 2020. b The infection rate of HBV in each region of Inner Mongolia in 2006. c The prevalence rate of HBsAg in each region of Inner Mongolia in 2020. d The prevalence rate of HBsAg in each region of Inner Mongolia in 2006.



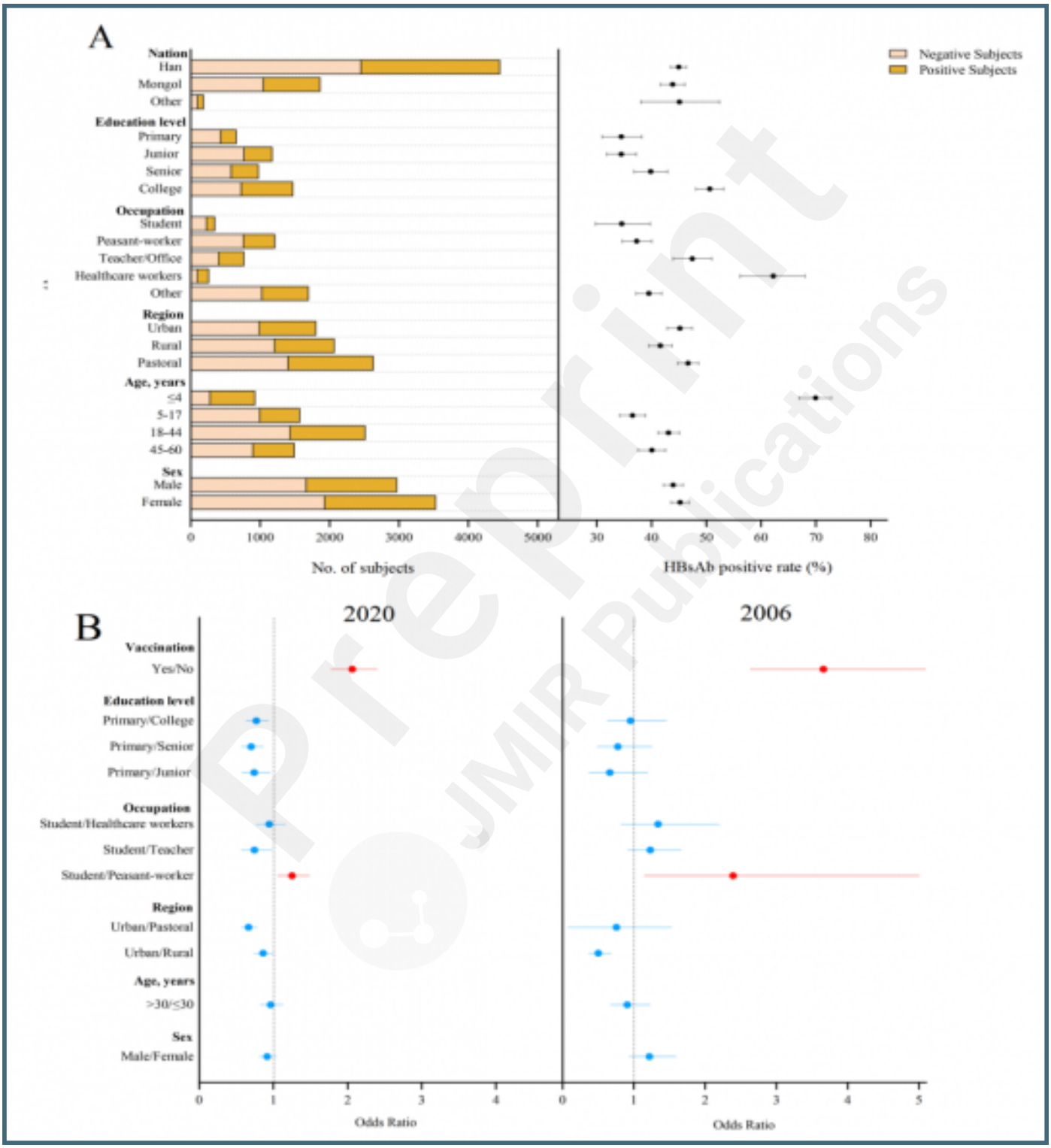
The infection rate of HBV in different subjects in 2020 and possible factors related to HBV infection in 2020 and 2006 of Inner Mongolia. a The positive result and 95% CI for positive rate of HBV in different subjects of Inner Mongolia in 2020. b The possible factors related to HBV infection in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.



The prevalence of HBsAg in different subjects in 2020 and the possible factors related to prevalence of HBsAg in 2020 and 2006 of Inner Mongolia. a The positive result and 95% CI for positive rate of HBsAg in different subjects of Inner Mongolia in 2020. b The possible factors related to HBsAg prevalence in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.



The positive rate of HBsAb in different subjects in 2020 and the possible factors related to HBsAb positive in 2020 and 2006 of Inner Mongolia. a The positive result and 95% CI for positive rate of HBsAb in different subjects of Inner Mongolia in 2020. b The possible factors related to HBsAb positive in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.



The positive rate of HBcAb in different subjects in 2020 and the possible factors related to HBcAb positive in 2020 and 2006 of Inner Mongolia. a The positive result and 95% CI for positive rate of HBcAb in different subjects of Inner Mongolia in 2020. b The possible factors related to HBcAb positive in 2020 and 2006 including red means risk factors and blue means protective factors or vitiating factors.