Economic-related inequalities in hepatitis B virus infection among 115.8 million pregnant women in China from 2013 to 2020

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Summary

Background Hepatitis B virus (HBV) infection is a serious global health problem and China has the largest disease burden. Literatures focusing on economic-related inequalities in HBV infection among pregnant women are scarce. We aimed to quantify the economic-related inequalities and the change over time in HBV infection among pregnant women in mainland China from 2013 to 2020 to inform strategies considering economic-related inequalities.

Methods We used national cross-sectional secondary data of pregnant women in 30 provinces from the National Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis and Hepatitis B Programme (iPMTCT Programme) from 2013 to 2020. We calculated concentration index and adjusted difference between the rich and the poor in the multivariable generalized estimating equation (GEE) model to measure economic-related inequality, after adjusted other risk factors.

Findings In this study, a total of 115,789,148 pregnant women of mainland China from 2013 to 2020 were included, the overall hepatitis B surface antigen (HBsAg) prevalence was 6.27% (95%CI: 6.26%-6.28%). The curve lay above the equality line, with the negative value of the concentration index of -0.027, which indicated that economic-related health disparities exist in the distribution of HBV infection and the inequality disadvantageous to the poor (propoor). The concentration index showed a trend of fluctuating decline, indicating that economic-related inequalities in HBsAg prevalence were narrowing. The adjust difference between counties with lowest economic level and counties with highest economic level (reference group) were 46.3% in HBsAg prevalence (all p < 0.05) in the multivariable GEE model, after controlling other confounders. A significant dose-response relationship was observed between low economic level and high HBsAg prevalence that the adjust difference increased from 15.6% (aOR=1.156, 95% CI: 1.064-1.257) in the high-economic group to 46.3% (aOR=1.463, 95% CI: 1.294-1.824) in the lowest-economic group, compared with the highest-economic group. The association between low economic level and high HBsAg prevalence was stable in the sensitivity analysis.

Interpretation HBV infection was more concentrated among population with lower economic status. Economicrelated inequalities in HBV infection decreased in the past decade. Our findings highlight the importance of developing equity-oriented policies and targeted interventions to reduce HBV infection among the poor and hard-to-reach populations to achieve the 2030 HBV elimination goals on time.

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Research in context

Evidence before the study

We searched PubMed and ScienceDirect for reports published in English or Chinese before January 1, 2022, with the terms "hepatitis B virus", "China", "economic", "inequality", and "pregnant women", to assess any research reporting economic-related inequalities in hepatitis B virus infection among pregnant women in China. We identified no national survey that reported economic-related inequalities in hepatitis B virus (HBV) infection among pregnant women in China.

Added value of this study

In this study, we assessed the economic-related inequalities and the change over time in HBV infection among pregnant women in mainland China from 2013 to 2020 to inform strategies considering economic-related inequalities. To our knowledge, this is the first study that assessed economic-related inequalities in HBV infection among pregnant women in China from 2013 to 2020. Our findings showed that HBV infection was more concentrated among population with lower economic status and economic-related inequalities in HBV infection decreased in the past decade.

Implications of all the available evidence

It is important to continue and optimize national programmes on prevention and treatment of hepatitis B to reduce economic-related inequalities in hepatitis B virus infection from a life cycle perspective. Our findings highlight the importance of developing equity-oriented policies and targeted interventions to reduce HBV infection among the poor and hard-to-reach populations to achieve the 2030 HBV elimination goals on time. Future research should explore the effective strategies to reduce economic-related inequalities in hepatitis B virus infection.

Introduction

Hepatitis B virus (HBV) infection is a serious global health problem. According to the WHO, it is estimated that 296 million people were living with chronic hepatitis B infection in 2019, with 1.5 million new infections each year and causing 820,000 deaths annually due to chronic liver diseases, such as cirrhosis and liver cancer.¹ In 2016, the World Health Assembly adopted the first Global health sector strategy on viral hepatitis, which sets targets (reducing new infections by 90% and HBV-related mortality by 65% in 2030 compared to the 2015 baseline) on combating hepatitis that aligned with those of the Sustainable Development Goals and highlighted the critical role of universal health coverage. In 2021, the 74th World Health Assembly adopted a previous decision of the Executive Board to request that Global Health Sector Strategies on HIV, viral hepatitis

and sexually transmitted infections are developed for the period 2022–2030. Countries are trying their best to achieving the global hepatitis elimination targets countdown to 2030 under the Sustainable Development Agenda but still face challenges.^{2,3}

Among all the transmission routes, the virus is most commonly transmitted from mother to child during birth and delivery, especially in high and intermediate endemic areas.¹ It is well-known that neonates who infect with HBV at birth are at 95% risk of developing chronic infection and at 15%–40% risk of developing cirrhosis and liver cancer.⁴ Besides this route, contacting with blood or other body fluids during sex with an infected partner can also transmit the virus.^{1,5} Thus, pregnant women are the key population on prevention of transmission to child and uninfected partner.

The prevalence of HBV infection varies greatly between countries and even within a country.⁶⁻⁸ Most previous studies reported the prevalence and risk factors of HBV infection in the general population or specific population, for example pregnant women,9 HIV/AIDS patients,¹⁰ HCV patients,¹¹ or health care workers.¹² It is important to recognize that national average data on HBV infection are inadequate measures for monitoring and evaluation the progress of global HBV elimination targets given the within-country inequalities. For example, in China, HBV infection varied from 0.3% in the general population aged 1-4 years to 4.4% in the population aged 15-29 years in 2014,7 and varied from 2.40% to 17.60% in different provinces among pregnant women in 2015.13 China launched a major healthcare reform in 2009 and pledged to provide all citizens with equal access to basic health care with reasonable quality and financial risk protection.¹⁴ It has made substantial progress in improving equal access to care and enhancing financial protection, especially for people of a lower socioeconomic status.¹⁴ According to the National Health Statistical Yearbooks in China, the number of licensed doctors and nurses per 1000 population has continuously increased from 4.25 in 2009 to 7.57 in 2020. However, gaps remain in quality of care, control of diseases, and efficiency in delivery.¹⁴ The inequality on preventing HBV infection to achieve universal health coverage is of great concern. Some literatures have reported the association between poor maternal-and-child health and the level of inequality, especially for economic-related inequality.^{15,16} However, literatures focusing on economic-related inequalities in hepatitis B virus infection among pregnant women are scarce.

In the present study, we aimed to quantify the economic-related inequalities in hepatitis B virus infection among pregnant women in mainland China, to provide baseline data on understanding current status in inequalities. We also assessed the change of economicrelated inequalities over time from 2013 to 2020, to inform targeted strategies considering economic-related inequalities in curbing HBV infection to achieve the 2030 HBV elimination goals on time.

Methods

Data source

The HBV-related secondary data used in this study was from the Management Information System of the National Integrated Prevention of Mother-to-Child Transmission of HIV, Syphilis and Hepatitis B Programme (iPMTCT Programme) from 2013 to 2020 in mainland China. The program was started in 2011 in 1156 (41%) county-level administrative units (briefly, counties) to prevent the PMTCT of Hepatitis B^{13,17} and was funded by the Government of China. Since 2015, the National iPMTCT Programme has expanded to all the 2856 counties in mainland China.¹⁸ Detailed design, organization, and implementation of this program are described elsewhere.^{17,19,20} Briefly, all the health-care facilities which provided antenatal care, labor or delivery services in mainland China were required to participated in the program following the protocol and implementation plan of the national iPMTCT Programme issued by the National Health Commission. Hepatitis B surface antigen (HBsAg) was required to be tested among pregnant women during antenatal care according to the standardized procedures. Aggregated data on HBV infection among women accessing antenatal care services were reported through the system on a monthly basis. The entry of data was done at county level. The quality of data was re-checked at higher administrative levels, following the national protocol and guidelines. All the HBV data were collected by the Management Information System, a routine reporting system of the National iPMTCT Programme.²⁰

Other data was from the National (Health) Statistical Yearbooks in China from 2013 to 2020. We extracted county-level and province-level economic status, sociodemographic status, health resource, and healthcare factors from the statistics yearbooks, including GDP per capita, proportion of female illiterates aged 15 years or over, proportion of total health expenditure in GDP, number of licensed doctors and nurses per 1000 population, proportion of maternal systematic management, and number of livebirths per 10 000 population.

In the present study, we included all the pregnant women who were tested for hepatitis B surface antigen (HBsAg) in the National iPMTCT Programme from 2013 to 2020. Peking University institutional review board (IRB) waived ethical review for the analysis of secondary aggregated data. Patient consent were obtained in the National iPMTCT Programme. From 2013 to 2020, there were 122.67 million pregnant women in mainland China. Among them, there were a total of 115.79 million (94.39%) pregnant women tested for HBsAg in the National iPMTCT Programme during 2013–2020, who were all included in the final analysis.

Measures of HBV infection

During antenatal care, pregnant women were tested for HBsAg. Enzyme-linked immunosorbent assays (ELISA) was recommended to detect seropositivity of HBsAg in pregnant women following the implementation plan for the National iPMTCT Programme. All the serological tests were conducted at the local qualified hospital laboratories as routine medical services. An External Quality Assessment (EQA) was conducted every year by the National Center for Clinical Laboratories for quality control.

HBV infection was defined as being tested seropositive for HBsAg in this study.^{2,19} According to the WHO, endemicity of HBV infection were defined by the prevalence of HBsAg as low endemic (< 2%), lower intermediate endemic (2–4.99%), higher intermediate endemic (5–7.99%) and high endemic (\geq 8%), which were consistent with previous studies.^{6,21}

Measures of economic-related inequality

We assessed the economic-related inequality in HBV infection by calculating concentration index (C) and Lorenz curve.^{22,23} In this study, the distribution of HBV infection was examined by economic status quintiles. Economic status was defined by dividing GDP per capita into quintiles (lowest, low, middle, high, highest). The C is defined as twice the area between the concentration curve and the line of equality. The Lorenz curve is obtained by plotting the cumulative percentage of HBV infection (Yaxis) against the cumulative percentage of the population ranked by economic status (X-axis). The C can be calculated using the following formula²⁴

$$C = \frac{2}{\mu \times cov(h, r)}$$

where h refers to the health outcome (HBV infection), μ is the mean of h, and r denotes the fractional rank of individuals in the distribution used (economic status quintiles). The concentration index ranges between -I and +I. A value of zero for concentration index represents absolute fairness and there exists no economic -related inequality. If the concentration index takes a negative value, indicating HBV infection is more concentrated among poor people (pro-rich). Conversely, if concentration index is a positive value, it indicates that HBV infection is more concentrated among rich people (pro-poor).

Besides concentration index (C) and Lorenz curve, we calculated adjusted difference between the highest economic level (reference group) and other groups of economic levels (lowest, low, middle, or high) in the multivariable generalized estimating equation model to measure economic-related inequality, after adjusted other risk factors.

Statistical analysis

The total prevalence of HBsAg and its 95% confidence intervals (CIs) was calculated as well as by different

sociodemographic status, health resource, and healthcare characteristics groups. In the univariable analysis, nonparametric tests were used to compare the demographic status, health resource and healthcare characteristics by different economic status. Trends of HBsAg prevalence from 2013 to 2020 were calculated by Cochran-Armitage test for trend. The prevalence of HBV infection in different regions were compared by Chi-square tests. To show the trend and annual change over a specified time interval, we further calculated the estimated annual percentage change (EAPC). A regression line was fitted to the natural logarithm of HBV prevalence using the formula: $y = \alpha + \beta x + \varepsilon$, where x is calendar year and y refers to ln (HBsAg prevalence). EAPC was calculated as 100 \times (e^{β}- 1) and its 95% CIs were calculated. If the EAPC estimation and its 95% CIs were both > 0 (or both < 0), HBV prevalence was indicated to be in an increasing trend (or a decreasing trend) in the given time interval. Concentration index was calculated and Lorenz curve was drawn to examine the economic-related inequality in HBV infection.

In the multivariable analysis, generalized estimating equation (GEE) models were applied to estimate the association between economic-related inequality and HBV infection, which dedicated for analysis of longitudinal data with repeated measures over time. We used the GEE model with a negative binomial distribution and log link function to control for the skewed nature of variables. We calculated adjusted association (adjusted odds ratio, aOR) between economic levels and HBV infection after controlling other confounding factors, including the effect of time, demographic status, health resource, and healthcare factors. The adjusted odds ratio (aOR) with 95% confidence interval (CI) were calculated. To examine the robust of the results, we applied sensitivity analysis by including economic status (GDP per capita) as continuous variable in the GEE model, instead of categorical variable. Two-sided p values of lower than 0.05 were considered to be statistical significance. All data analysis were done with SPSS version 23.0 and Stata version 17.0 software.

Role of the funding source

The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had access to all data in the study and had final responsibility for the decision to submit for publication.

Results

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Comparison of basic characteristics by economic status Table I outlines sociodemographic status, health resource, and healthcare characteristics by different economic status. Provinces with lower economic level were more likely to have higher proportion of female illiterates aged 15 years or over, higher proportion of total health expenditure in GDP, lower numbers of licensed doctors and nurses, lower proportion of maternal systematic management, higher numbers of livebirths (all p<0.05, Table I).

Time trends and provincial disparities in HBsAg prevalence in China

A total of 115,789,148 pregnant women in 30 provinces of Mainland China from 2013 to 2020 were included in this study, and 7266,143 were HBsAg positive, indicating an overall HBsAg prevalence of 6.27% (95%CI: 6.26%-6.28%) among adult women in China between 2013 and 2020. HBsAg prevalence decreased significantly from 2013 to 2020 (p for trend <0.001).

Provincial disparities in HBsAg prevalence among pregnant women in China were narrowing (HBsAg prevalence ranged from 1.78% to 22.35% in 2013 and ranged from 1.88% to 11.99% in 2020), but disparities still exist (Figure 1). The top 5 provinces with the highest disease burden of HBV infection in China were all observed significantly declines, with EAPC of -76.12%(95%CI: -82.53% to -67.36%) in Hainan, -56.2%(95%CI: -60.52% to -51.41%) in Jiangxi, -54.99%(95%CI: -63.62% to -44.32%) in Guangdong, -50.21% (95%CI: -155.94% to -43.73%) in Fujian, -14.67% (95%CI: -17.59% to -11.65%) in Guangxi.

Economic-related inequalities in HBsAg prevalence in China

The Lorenz curve of HBV infection pregnant women is shown in Figure 2. The curve lay above the equality line, with the negative value of the concentration index of -0.027, which indicated that economic-related health disparities exist in the distribution of HBV infection and the inequality disadvantageous to the poor (pro-poor) that HBV infection was more concentrated among population with lower economic status (Figure 2). The negative correlation of HBsAg prevalence and economic status were observed in western and eastern areas, but not in central area (supplemental figure 1). The concentration index showed a trend of fluctuating decline (from -0.0619 in 2013 to -0.0004in 2020, Figure 3), indicating that economic-related inequalities in HBsAg prevalence were narrowing.

Association between economic level and HBsAg prevalence in the GEE model

In the multivariable GEE model, economic level was inversely correlated with HBsAg prevalence (p<0.05, Table 2). The adjust difference between counties with lowest economic level and counties with highest economic level (reference group) were 46.3% in HBsAg prevalence (all p<0.05), after controlling other

			Economic status (95% (c) a		p value
	Lowest	Low	Middle	High	Highest	
Number of livebirths (per 10 000 population)	42.2 (18.2–62.7)	40.6 (12.9–71.7)	35.6 (11.3–66.4)	31.6 (20.8–65.0)	21.6 (13.1–59.1)	<0.001*
Proportion of maternal systematic management (%)	90.8 (85.9–93.8)	87.2 (84.7—91.9)	91.3 (87.8–94.0)	92.1 (91.4–93.2)	95.9 (93.1–96.4)	<0.001*
Proportion of total health expenditure in GDP (%)	8.2 (7.2–9.8)	6.8 (6.1–8.8)	6.9 (6.2–8.0)	5.9 (4.9–6.4)	5.2 (4.3-6.4)	<0.001*
Number of licensed doctors and nurses per 1000 population	5.9 (4.9–6.5)	5.7 (5.3–6.7)	6.3 (5.8–7.1)	6.5 (5.9–7.1)	7.3 (6.5–8.4)	<0.001*
Proportion of female illiterates aged 15 years or over (%)	11.8 (4.4–15.7)	7.4 (4.7–10.6)	6.5 (4.6–9.7)	6.2 (4.6-8.2)	5.7 (3.3–8.5)	<0.001*
Table 7: Comparison of demographic status, health resourd Economic levels were defined by dividing GDP per capita into quint Data was mesented as median with intercuartle rance.	ce, and healthcare charac iles (lowest, low, middle, hig	teristics by different ecc h, highest).	nomic status from 2013	: to 2020.		

confounders. A significant dose-response relationship was observed between low economic level and high HBsAg prevalence that the adjust difference increased from 15.6% (aOR=1.156, 95% CI: 1.064-1.257) in the high-economic group to 46.3% (aOR=1.463, 95% CI: 1.294-1.824) in the lowest-economic group. Moreover, the number of licensed doctors and nurses per 1000 population (aOR=0.945, 95% CI: 0.912-0.978), and year (aOR=0.952, 95% CI: 0.941-0.963) were also associated with HBsAg prevalence (all p < 0.05). The association between low economic level and high HBsAg prevalence was stable in the sensitivity analysis (supplemental Table 1).

Discussion

To our knowledge, this is the first study that assessed economic-related inequalities in HBV infection among pregnant women in China from 2013 to 2020. China has the world's largest burden of HBV infection and is a major contributor towards the global elimination of hepatitis B disease by 2030. Using data from the National iPMTCT Programme and National Statistical Yearbook, we reported the trends of HBsAg prevalence and economic-related inequalities in HBV infection among 115.8 million pregnant women in mainland China between 2013 and 2020. We found that HBV infection was more concentrated among pregnant women with lower economic status and economicrelated inequalities in HBV infection decreased in the past decade. China was among the first developing countries to enact a universal hepatitis B vaccination program for newborns and infants in 1992.³ However, parents had to pay out of pocket. China has integrated hepatitis B vaccine into the national expanded program on immunization and provided free vaccination since 2002.3 The Chinese government collaborated with Global Alliance for Vaccine and Immunization (GAVI) to provide free hepatitis B vaccine in the poor regions to work against inequalities in terms of hepatitis B vaccine coverage.³ The gap between the rich and the poor was reduced by the implementation of these comprehensive interventions. It is worth noting that economic-related inequalities still exist within a country with the largest adjust difference as 46.3% between the poor and the rich, although much progress has been made on HBV prevention and control.

We also found that provincial disparities in HBsAg prevalence among pregnant women in China were narrowing. In 2013, the province with the highest prevalence of HBsAg (22.35%) were nearly 20 times higher than in the province with the lowest prevalence of HBsAg (1.78%). In 2020, the province with the highest prevalence of HBsAg (1.99%) were nearly 10 times higher than in the province with the lowest prevalence of HBsAg (1.88%). Five years after the implementation of the global health sector strategy on viral hepatitis to

p<0.05. 95% CI, 95% confidence interval

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					Yea	irs				
		2013	2014	2015	2016	2017	2018	2019	2020	
Western	Qinghai –	1.78	4.26	4.25	4.57	4.87	5.84	5.92	6.90	
	Xinjiang-	3.17	3.27	3.33	3.74	3.82	4.15	4.06	3.60	
	Yunnan-	2.84	4.36	4.78	4.55	3.97	3.41	3.25	3.40	
	Guizhou –	5.66	5.58	5.53	5.14	5.03	4.87	4.49	4.25	
	Gansu-	3.92	4.03	4.32	3.98	4.28	4.10	3.96	3.78	 5
	Inner Mongolia-	2.95	2.95	3.06	2.84	3.01	2.77	2.51	2.51	
	Sichuan-	7.92	7.46	7.22	6.80	6.77	6.69	6.29	6.14	
	Ningxia-	6.79	6.20	5.83	5.17	4.88	4.39	4.07	3.62	
	Chongging-	7.18	6.95	6.68	6.27	6.13	6.05	5.82	5.46	
	Guanaxi-	11.00	10.74	10.84	10.54	10.50	10.26	10.07	9.84	
Centra I I	Shaanxi-	7.38	6.85	6.55	5.57	5.36	4.60	3.91	3.81	
	Heilongijang	4.94	5.51	5.27	4 76	4.26	3.89	3.59	3.32	 10
	⊓unan=	8.07	8.41	8 19	7.59	7.50	7 30	7 16	6.99	Ξ
	Snanxi- Hunan-	3.04	2.88	3.07	4.34	4.09	3.02	3.50	3.41	3sA(
	Annui-	6.35	6.00	5.69	5.15	4.81	4.45	4.12	3.99	g pre
	Henan-	6.12	6.04	5.48	4.53	4.33	4.03	3.92	3.79	eval
	Jiangxi-	16.28	15.05	14.73	13.42	12.35	11.90	11.10	10.56	ence
	Hubei-	6.26	6.28	6.32	6.16	6.20	6.16	5.69	5.20	%) e
-	Hainan-	22.35	19.29	17.60	15.94	14.98	13.35	12.48	11.99	 15
	Hebei-	3.50	3.28	3.89	3.40	3.19	2.98	2.84	2.73	
	Fujian-	15.25	13.64	13.21	12.21	11.91	11.22	10.57	9.97	
	Guangdong-	15.37	13.41	12.43	11.30	11.02	10.43	9.75	9.30	
Ea:	Shandong-	4.49	4.49	4.63	4.09	4.08	3.84	3.45	3.10	
ster	Liaoning-	3.86	3.46	3.71	3.28	3.26	2.97	2.89	2.70	
	Tianjin-	2.41	2.18	2.40	2.09	2.08	2.02	1.88	1.97	
	Beijing-	3.54	3.20	3.59	3.19	3.14	3.09	2.79	2.51	20
	Zhejiang-	6.88	7.04	6.74	6.17	6.15	5.75	5.35	5.15	
	Shanghai-	4.72	4.40	4.32	3.90	4.08	4.02	3.74	3.72	
	Jiangsu-	4.13	4.85	4.56	4.54	4.33	4.09	3.71	3.57	

Figure 1. Time trends and provincial disparities in HBsAg prevalence among pregnant women in 30 provinces of mainland China from 2013 to 2020.

HBsAg prevalence decreased significantly from 2013 to 2020 (p for trend <0.001). Provincial disparities in HBsAg prevalence among pregnant women in China were narrowing (HBsAg prevalence ranged from 1.78% to 22.35% in 2013 and ranged from 1.88% to 11.99% in 2020), but disparities still exist. HBsAg - hepatitis B surface antigen.

eliminate HBV as a public health threat by 2030 and the publication of the Healthy China 2030 blueprint in 2016, China has focused more on public health and disease prevention,²⁵ especially for the major infectious disease (such as HBV). The country has made good progress in reducing incidence of HBV infection in the past three decades, which are mainly due to high vaccination coverages among children and high coverage of timely birth-dose vaccine for prevention of mother-to-child transmission of HBV. 3

In the present study, a significant dose-response relationship was observed between low economic level and high HBsAg prevalence. The economic-related inequalities were also observed in other health domains and health services.^{26,27} The Chinese government has always attached great importance to the health of all the

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Figure 2. Lorenz curve of HBV infection.

The Lorenz curve of HBV infection lay above the equality line, with the negative value of the concentration index of -0.027 (p < 0.05), indicating that economic-related health disparities exist in the distribution of HBV infection. HBV infection was more concentrated among population with lower economic status. HBV – hepatitis B virus.



Figure 3. Trends of concentration index on HBsAg prevalence from 2013 to 2020.

The concentration index showed a trend of fluctuating decline (from -0.0619 in 2013 to -0.0004 in 2020), that economic-related inequalities in HBsAg prevalence were narrowing (p<0.05). HBsAg - hepatitis B surface antigen.

Factors	aOR	Lower Confidence Interval	Upper Confidence Interval	P value
Economic level				
Lowest	1.463	1.294	1.824	<0.001*
Low	1.387	1.172	1.641	<0.001*
Middle	1.157	1.002	1.334	0.046*
High	1.156	1.064	1.257	0.001*
Highest	1 (Reference)			
Year	0.952	0.941	0.963	0.020*
Proportion of total health expenditure in GDP (%)	0.966	0.915	1.020	0.216
Region				
Eastern	1 (Reference)			
Central	0.968	0.569	1.647	0.904
Western	1.023	0.606	1.726	0.934
Proportion of female illiterates aged 15 years or over (%)	0.993	0.965	1.021	0.623
Number of licensed doctors and nurses per 1000 population	0.945	0.912	0.978	0.001*
Proportion of maternal systematic management (%)	1.000	0.994	1.006	0.957

Table 2: Association between economic level and HBsAg prevalence in the multivariable GEE model.

* p<0.05; aOR, adjusted odds ratio.

Chinese people and promoted universal health coverage. For example, China began to provide all the Chinese people with free basic public health services to promote the equity of health services and further improve the health of residents since 2009, which is socalled the Basic Public Health Services (BPHS) program. However, inequalities still exist. Wang et al.²⁶ reported that there existed sociodemographic disparities in the establishment rate of health records and inequalities in the utilization of health records services among 0.5 million migrants in China.

Since the publication of the Healthy China 2030 blueprint in 2016, the Chinese Government has accelerated to transform its development paradigm, that it has shifted its goal from the efficiency-orientation model towards one which prioritizes social equity and sustainability.²⁸ The national iPMTCT Programme and other programmes (for example BPHS) guarantee the provision of health services in China to prevent new infections and reduce HBV-related deaths. However, according to the data from 2017 Migrant Population Dynamic Monitoring Survey in China, HepB vaccination rate was 59.08% among migrant population and migrants from urban regions had a higher vaccination rate than those from rural regions.²⁹ Given the countdown of 2030 hepatitis elimination goal, more efforts are needed to promote the services on prevention HBV infection and deaths in the hard-to-reach population and areas to reduce the inequalities, such as floating population and rural poor areas. For example, how to provide continuous, whole-course and standardized prevention mother-to-child transmission service for floating population among pregnant women is an urgent and important issue at present in the national iPMTCT Programme. Similarly, in the clinical diagnosis and treatment process of patients infected with HBV, how

to provide more accessible and continuous health services for low-income people is also an urgent issue to improve the diagnosis and treatment coverage in the future.

As for economic-related inequalities, a variety of poverty-reduction health policies and programmes have been launched in impoverished areas in China, which have substantially improved the general health of the poorest with some success.^{28,30} However, there was no clear plan or action to monitor health equity, particularly in populations with different socioeconomic positions.²⁸ As for the Healthy China 2030 plan by the Chinese government and the 2030 HBV elimination targets by WHO, many indicators have been proposed to improve input and targeted outcomes. However, these indicators were mostly related to the measurement of aggregated health status and inadequate attention was paid to the distribution of health indicators among populations with different socioeconomic level within a country.²⁸ This could potentially undermine the efforts by the country to alleviate inequalities in HBV infection. The monitoring framework on economic-related inequalities in HBV infection should not be ignored. In addition, we found that the negative correlation of HBsAg prevalence and economic status were observed in western and eastern areas, but not in central area. One explanation was that central region was in the middle level of GDP as well as HBsAg prevalence in China, compared with western and eastern region. Economic-related inequality might not be the key factor for HBV infection in central region, which was different from the rich eastern and poor western area. Our findings indicated that economic-related inequality should be paid more attention on western and eastern areas.

There were several limitations in this study. First, this is an ecological study by linking aggregated data on

HBV infection and statistical yearbook at county-level that there could be ecological fallacies. Ecological fallacies might exist when use aggregated data instead of individual data. We used county-level and province-level economic status from statistical yearbook, given that the national iPMTCT Programme did not collect individual information on household income for each HBVinfected pregnant woman. Second, aggregated data on HBV infection were collected instead of individual data in the national iPMTCT Programme. Other potential confounders (such as individual behavior, age, vaccination status, multiple pregnancies, sensitivity and specificity of the HBsAg test) could not be included in the GEE model. Third, other HBV biomarkers were not collected in the national iPMTCT Programme (such as HBV DNA). We could not do further analysis because of the limitation of the data. Fourth, the National iPMTCT Programme was started in half of all counties in 2011 and expanded to all the counties in mainland China in 2015. The change of the coverage on program might have potential impact on association of HBV infection and economic-related inequalities.

In conclusion, HBV infection was more concentrated among population with lower economic status and economic-related inequalities in HBV infection decreased in the past decade. However, the inequalities still exist. Our findings highlight the importance of developing equity-oriented policies and targeted interventions to reduce HBV infection among the poor and hard-to-reach populations to achieve the 2030 HBV elimination goals on time.

Contributors

Ailing Wang and Min Liu conceived the study, designed the study, collected the data, supervised the study, and interpreted the results. Jue Liu searched the literature, analyzed the data and wrote the draft manuscript. Xiaoyan Wang collected the data and wrote the draft manuscript. XW and JL contributed equally and were the co-first authors. Xiaoyan Wang, Jue Liu, Qian Wang, Yaping Qiao, Xi Jin, Zhixin Li, Wenzhan Jing, Min Du, Wenxin Yan, Ailing Wang, and Min Liu revised the manuscript. All authors contributed to writing the manuscript, and approved the final version for manuscript.

Data sharing statement

Datasets generated and/or analyzed in the present study are available from the corresponding author upon reasonable request.

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Declaration of interests

The authors have nothing to declare.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi: 10.1016/j. eclinm.2022.101465.

References

- I Hepatitis B. Geneva: World Health Organization; 2017. [internet]. Available from: https://www.who.int/news-room/fact-sheets/ detail/hepatitis-b. [cited 2021 Dec 30].
- detail/hepatitis-b. [cited 2021 Dec 30].
 Global Progress Report On HIV, Viral Hepatitis and Sexually Transmitted infections, 2021-Accountability For the Global Health Sector Strategies 2016-2021. Actions For Impact. Geneva: World Health Organization; 2021. [internet]. Available from: https://apps.who.int/iris/rest/hitstreams/1248210/retrieve_fride 2021 Dec 30]
- int/iris/rest/bitstreams/1348210/retrieve. [cited 2021 Dec 30].
 Liu J, Liang W, Jing W, Liu M. Countdown to 2030: eliminating hepatitis B disease, China. Bull World Health Organ. 2019 Mar 1;97(3):230–238. https://doi.org/10.2471/blt.18.219469. PMID:30992636.
 Jing W, Liu J, Liu M. Eliminating mother-to-child transmission of
- 4 Jing W, Liu J, Liu M. Eliminating mother-to-child transmission of HBV: progress and challenges in China. Front Med. 2020 Feb;14(1):21– 29. https://doi.org/10.1007/S11684-020-0744-2. PMID:31974872.
- Liu J, Zhang S, Wang Q, et al. Prevalence of HBsAg/HBeAg amongst 1 936 801 couples preparing for pregnancy in rural China: an observational study. J Viral Hepat. 2017 Aug;24(8):679–686. https://doi.org/10.1111/jvh.12693. PMID:28199770.
- 6 Schweitzer A, Horn J, Mikolajczyk RT, Krause G, Ott JJ. Estimations of worldwide prevalence of chronic hepatitis B virus infection: a systematic review of data published between 1965 and 2013. Lancet. 2015 Oct 17;386(10003):1546–1555. https://doi.org/10.1016/ s0140-6736(15)61412-x. PMID:26231459.
- 7 Cui F, Shen L, Li L, et al. Prevention of Chronic Hepatitis B after 3 Decades of Escalating Vaccination Policy, China. *Emerg Infect Dis.* 2017 May;23(5):765–772. https://doi.org/10.3201/eid2305.161477. PMID:28418296.
- 8 Liu J, Zhang S, Wang Q, et al. Seroepidemiology of hepatitis B virus infection in 2 million men aged 21-49 years in rural China: a population-based, cross-sectional study. *Lancet Infect Dis.* 2016 Jan;16(1):80–86. https://doi.org/10.1016/S1473-3099(15)00218-2. PMID:26268687.
- Liu J, Liu J, Liu M, Pang Q, Wen Y. Prevalence of hepatitis B virus infection and its associated factors among 15,461 pregnant women in Yunnan province, China. Ann Epidemiol. 2020 Sep;49:13–19. https://doi.org/10.1016/j.annepidem.2020.05.011. PMID:32951803.

- IO Singh KP, Crane M, Audsley J, Avihingsanon A, Sasadeusz J, Lewin SR. HIV-hepatitis B virus coinfection: epidemiology, pathogenesis, and treatment. Aids. 2017 Sep 24;31(15):2035–2052. https://doi.org/ 10.1097/qad.0000000001574. PMID:28692539.
- II Liu CJ, Chen PJ. Changing epidemiology of liver disease in Asia: dual infection of HBV and HCV. *Liver Int.* 2021 Aug 17. https:// doi.org/10.1111/liv.15040. PMID:34402183.
- 12 Wijayadi T, Sjahril R, Turyadi, et al. Seroepidemiology of HBV infection among health-care workers in South Sulawesi, Indonesia BMC Infect Dis. 2018 Jun 18;18(1):279. https://doi.org/10.1186/ s12879-018-3190-x. PMID:29914398.
- 13 Liu J, Wang X, Wang Q, et al. Hepatitis B virus infection among 90 million pregnant women in 2853 Chinese counties, 2015-2020: a national observational study. *Lancet Reg Health West Pac.* 2021 Nov;16: 100267. https://doi.org/10.1016/j.lanwpc.2021.100267. PMID:34590067.
- 14 Yip W, Fu H, Chen AT, et al. 10 years of health-care reform in China: progress and gaps in Universal Health Coverage. *Lancet.* 2019;394(10204):1192–1204. https://doi.org/10.1016/S0140-6736 (19)32136-1.
- 15 Kim R, Rajpal S, Joe W, et al. Assessing associational strength of 23 correlates of child anthropometric failure: an econometric analysis of the 2015-2016 National Family Health Survey, India. Soc Sci Med. 2019 OCt;238: 112374. https://doi.org/10.1016/j.socscimed.2019.112374. PMID:31345611.
- 16 Gao Y, Zhou H, Singh NS, et al. Progress and challenges in maternal health in western China: a Countdown to 2015 national case study. Lancet Glob Health. 2017 May;5(5):e523-e536. https://doi. org/10.1016/s2214-109X(17)30100-6. PMID:28341117.
- 17 Wang AL, Qiao YP, Wang LH, et al. Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. *Bull World Health Organ*. 2015 Jan 1:93(1):52–56. https://doi.org/10.2471/blt.14.139626. PMID:25558108.
- 18 Qiao YP, Su M, Song Y, et al. Outcomes of the national programme on prevention of mother-to-child transmission of hepatitis B virus in China, 2016-2017. *Infect Dis Poverty*. 2019 Aug 5;8(1):65. https:// doi.org/10.1186/s40249-019-0576-y. PMID:31378202.
- 19 National Health Commission. Protocol For Prevention of Mother-To-Child trans- mission of HIV, Syphilis and Hepatitis B. Beijing: Ministry of Health; 2011. [internet]. Available from: http://www.moh. gov.cn/cmsresources/mohfybjysqwss/cmsrsdocument/doc11298. doc. [cited 2021 Dec 29].
- 20 National Health and Family Planning Commission. Implementation Plan for the Prevention of Mother-To-Child Transmission of AIDS,

Syphilis and Hepatitis B (2015). Beijing: National Health and Family Planning Commission; 2015. [internet]. Available from: http:// www.nhc.gov.cn/fys/s3581/201506/4f2123fa955a44afa75a75da2ad35d6e.shtml. [cited 2021 Dec 29].

- 21 Global Health Sector Strategy on Viral Hep- atitis, 2016-2021. Geneva: World Health Organization; 2021. [internet]. Available from: https://www.who.int/publications/i/item/WHO-HIV-2016.06. [cited 2021 Dec 29].
- 2 Lerman RI, Yitzhaki S. Income inequality effects by income source: a new approach and applications to the United States. *Rev Econ Stat.* 1985:151–156.
- 23 Lopez-Feldman A. Decomposing inequality and obtaining marginal effects. Stata J. 2006;6(I):106-111.
- 24 O'Donnell O, Van DE, Wagstaff A, Lindelow M. Analyzing Health Equity Using Household Survey Data. Washington: World Bank Institute; 2008. World Bank Publications [internet]. Available from: https://openknowledge.worldbank.org/bitstream/handle/ 10986/6896/4248001SBN9780110FFICIALOUSE00NLY10. pdf?sequence=r&isAllowed=y. [cited 2021 Dec 29].
- 25 Chen P, Li F, Harmer P. Healthy China 2030: moving from blueprint to action with a new focus on public health. *Lancet Public Health.* 2019 Sep;4(9):e447. https://doi.org/10.1016/s2468-2667 (19)30160-4. PMID:31493840.
- 26 Wang J, Zhu J, Wang X, Che Y, Bai Y, Liu J. Sociodemographic disparities in the establishment of health records among 0.5 million migrants from 2014 to 2017 in China: a nationwide cross-sectional study. Int J Equity Health. 2021 Dec 2;20(1):250. https://doi.org/10.1186/S12939-021-01584-2. PMID:34856984.
- 27 Li Z, Kim R, Subramanian SV. Economic-related inequalities in child health interventions: an analysis of 65 low- and middleincome countries. Soc Sci Med. 2021 May;277: 113816. https://doi. org/10.1016/j.socscimed.2021.113816. PMID:33848717.
- 28 Wang Z, Yang G, Guo Y. Harnessing the opportunity to achieve health equity in China. Lancet Public Health. 2021 Dec;6(12):e867–e868. https://doi.org/10.1016/s2468-2667(21)00211-5. PMID:34838190.
- 29 Wang J, Zhu J, Bai Y, Wang X, Che Y, Liu J. Vaccination rates and determinants of nine recommended vaccines among migrants in China: a nationwide cross-sectional study. *Hum Vaccin Immunother*. 2021 OCt 6:1–9. https://doi.org/10.1080/21645515. 2021.1981088. PMID:34614381.
- 30 Robert L. Poverty Alleviation Via Healthcare. Beijing: China Global Television Network; 2019. [internet]. Available from: https://news. cgtn.com/news/2019-10-17/Poverty-alleviation-via-healthcare-KQ2aiQGjiE/index.html. [cited 2021 Dec 31].