

Supplemental Online Content

Wu H, Yang Y, Jia J, et al. Maternal preconception hepatitis B virus infection and risk of congenital heart diseases in offspring among Chinese women aged 20 to 49 years. *JAMA Pediatr*. Published online March 13, 2023. doi:10.1001/jamapediatrics.2023.0053

eTable 1. Classification of Hepatitis B Virus Infection Status

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Classification of Hepatitis B Virus Infection Status

Abbreviations: HBsAg, hepatitis B surface antigen; HBsAb, hepatitis B surface antibody; HBeAg, hepatitis B envelop antigen; HBeAb, hepatitis B envelop antibody; HBcAb, hepatitis B core antibody; HBV, hepatitis B virus; +, positive; -, negative.

Group	Hepatitis B serological markers				
	HBsAg	HBsAb	HBeAg	HBeAb	HBcAb
Uninfected	-	-	-	-	-
	-	+	-	-	-
Previous infection	-	-	-	+	-
	-	-	-	+	+
	-	-	-	-	+
	-	+	-	+	-
	-	+	-	+	+
	-	+	-	-	+
New HBV infection	+	-	-	-	-
	+	-	-	+	-
	+	-	-	-	+
	+	-	-	+	+
	+	-	+	-	-
	+	-	+	-	+
	+	+	+	+	+
	+	+	-	+	+
	+	+	+	-	+
	+	+	+	+	-
	+	+	-	-	+
	+	+	-	+	-
	+	+	+	-	-
	+	+	-	-	-

eTable 2. Definition and Classification of Covariates

Covariates	Definition
Demographic and sociological covariates:	
Maternal age at LMP	Calculated by the date of last menstrual period minus the date of birth.
Paternal age at LMP	Calculated by the date of last menstrual period minus the date of birth.
Time interval between examination and LMP	Calculated by the date of last menstrual period minus the date of examination (within 6 months; 6 months to 1 year)
Maternal nationality	Self-reported (Han; minorities)
Maternal drinking	Self-reported (Yes; no)
Maternal smoking	Self-reported (Yes; no)
Maternal preconception harmful exposure	Exposure history of radial, the high temperature, pesticide, new decoration, paint, other organic solvents, fever, common cold, or passive smoking
History of adverse pregnancy outcome	Self-reported, including spontaneous abortion, induction abortion, or preterm birth (Yes; no)
Family history of congenital heart diseases (parental)	Self-reported (Yes; no)
Parity	Whether have previous live birth or stillbirth or not (Nulliparous; multiparous)
Maternal folic acid intake	Self-reported (Yes; no)
Early pregnancy common cold	Self-reported (Yes; no)
Early pregnancy passive smoking	Self-reported (Yes; no)
Early pregnancy medication	Self-reported (Treatment use; no use)
Preconception clinical covariates:	
BMI	Calculated by dividing the weight in kilogram by the square of the height in meter (underweight, <18.5 kg/m ² ; normal, 18.5-23.9 kg/m ² ; overweight, 24.0-27.9 kg/m ² ; obesity, ≥28.0 kg/m ²)
Diabetes	Self-reported or fasting plasma glucose ≥ 6.1 mmol/L (Yes; no)
Hypertension	Self-reported or systolic blood pressure ≥ 140 mm Hg, and (or) diastolic blood pressure ≥ 90 mm Hg (Yes; no)
Other infection	Women infected with Neisseria gonorrhoeae, Chlamydia trachomatis, Toxoplasma gondii, Cytomegalovirus, Treponema pallidum, or Rubella virus, by detecting their specific-serum antibodies. (Yes; no)
Paternal serum HBsAg status	Positive; negative.
Paternal HBV infection status	Males were also classified into 3 groups, which were similar to the classification of maternal preconception HBV infection status. (Uninfected, previous infection, and new infection)

Abbreviations: LMP, last menstrual period; BMI, body mass index; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus.

eTable 3. Baseline Characteristics of Female Participants in the Cohort Before and After Propensity Score Matching

	Before matching			After matching		
	HBV infected (n = 739,008)	Uninfected (n = 6,659,877)	Standardized difference ^a	HBV infected (n = 738,945)	Uninfected (n = 2,951,482)	Standardized difference ^a
Maternal age at LMP, years						
Mean (SD)	27.40 (4.36)	26.80 (4.26)	0.1376	27.40 (4.35)	27.30 (4.35)	0.0000
Median (IQR)	27 (24-30)	26 (24-29)		27 (24-30)	27 (24-30)	
Time interval between preconception examination and LMP						
Within 6 months	604,408 (81.79)	5,534,083 (83.10)	-0.0339	604,375 (81.79)	2,415,614 (81.84)	-0.0010
6 months to 1 year	134,600 (18.21)	1,125,794 (16.90)	0.0339	134,570 (18.21)	535,868 (18.16)	0.0010
Maternal preconception BMI						
Underweight, < 18.5 kg/m ²	118,923 (16.09)	862,023 (12.94)	0.0857	118,918 (16.09)	474,717 (16.08)	-0.0004
Normal, 18.5 to < 24.0 kg/m ²	513,517 (69.49)	4,719,439 (70.86)	-0.0299	513,516 (69.49)	2,053,856 (69.59)	-0.0004
Overweight, 24.0 to < 28.0 kg/m ²	82,865 (11.21)	851,313 (12.78)	-0.0497	82,865 (11.21)	3,31,700 (11.24)	-0.0003
Obesity, ≥ 28.0 kg/m ²	18,388 (2.49)	202,947 (3.05)	-0.0359	18,388 (2.49)	73,370 (2.49)	0.0004
Unknown	5,315 (0.72)	24,155 (0.36)	0.0422	5,258 (0.71)	17,839 (0.60)	0.0043
Preconception diabetes						
No	697,311 (94.36)	6,377,814 (95.76)	-0.0610	697,292 (94.36)	2,785,068 (94.36)	0.0022
Yes	37,726 (5.10)	250,020 (3.75)	0.0613	37,683 (5.10)	151,398 (5.13)	-0.0033
Unknown	3,971 (0.54)	32,043 (0.48)	0.0077	3,970 (0.54)	15,016 (0.51)	0.0030
Preconception harmful exposure						
No	623,733 (84.40)	5,869,233 (88.13)	-0.1027	623,729 (84.41)	2,495,225 (84.54)	-0.0008
Yes	102,054 (13.81)	697,606 (10.47)	0.0967	102,036 (13.81)	406,425 (13.77)	-0.0004
Unknown	13,221 (1.79)	93,038 (1.40)	0.0296	13,180 (1.78)	49,832 (1.69)	0.0032

	Before matching			After matching		
	HBV infected (n = 739,008)	Uninfected (n = 6,659,877)	Standardized difference ^a	HBV infected (n = 738,945)	Uninfected (n = 2,951,482)	Standardized difference ^a
Maternal preconception infectious status						
No	551,211 (74.59)	4,819,992 (72.37)	0.0509	551,206 (74.59)	2,205,054 (74.71)	-0.0011
Yes	146,604 (19.84)	1,569,214 (23.56)	-0.0934	146,604 (19.84)	586,231 (19.86)	0.0001
Unknown	41,193 (5.57)	270,671 (4.06)	0.0658	41,135 (5.57)	160,197 (5.43)	0.0019
Parity						
Nulliparous	437,463 (59.20)	3,967,948 (59.58)	-0.0078	437,428 (59.20)	1,747,177 (59.20)	-0.0001
Multiparous	301,545 (40.80)	2,691,929 (40.42)	0.0078	301,517 (40.80)	1,204,305 (40.80)	0.0001

Abbreviations: LMP, last menstrual period; SD, standard deviation; IQR, interquartile range; BMI, body-mass index; HBV, hepatitis B virus.

^aStandardized differences were calculated according to Austin¹.

1. Austin PC. Using the Standardized Difference to Compare the Prevalence of a Binary Variable Between Two Groups in Observational Research. *Communications in Statistics - Simulation and Computation*. 2009/05/14 2009;38(6):1228-1234. doi:10.1080/03610910902859574

eTable 4. Detailed Information on Previous Studies

Author (Year of publication)	Geographic Region	Study Design	Sample Size	Diagnosis Method of CHDs	Ascertainment of HBV Infection	Infection Time	ORs/RRs (95% CIs)
Liang ¹⁴ , 2017	China	Case-control	5,381	Not stated	Self-report	First trimester	1.38 (0.33-5.72)
Wang ¹⁶ , 2022	China	Cohort	44,048	Physical examination, heart auscultation, electrocardiogram, pulse oximetry, and echocardiography	Serological markers and HBV-DNA testing	First trimester	2.21 (1.66-2.95)
Lai ¹⁷ , 2001	China	Case-control	1,522	Not stated	Self-report	First trimester	1.1014 (0.4650-26,088)
Guo ¹⁸ , 2010	China	Case-control	367	Ultrasound examination	Antibody testing	First trimester	1,448.83 (6.37-329,730.35)

Abbreviations: CHDs, congenital heart diseases; HBV, hepatitis B virus; ORs, odds ratios; RRs, relative ratios.