GYNECOLOGY

Preconception blood pressure and time to pregnancy among couples attempting to conceive their first pregnancy

Xiang Hong, PhD[1]; Jun Zhao, PhD[1]; Kaiping Huang, MS; Qiaoyun Dai, MS; Hongguang Zhang, BS; Yan Xuan, PhD; Jingwei Wu, PhD; Shenghao Fang, MD; Qiaomei Wang, MD; Haiping Shen, MD; Zongyu Xu, MD; Yiping Zhang, MD; Donghai Yan, MD; Daxun Qi, MS; Xueying Yang, BS; Yue Zhang, MS; Xu Ma, MS; Bei Wang, PhD

BACKGROUND: The association of abnormal blood pressure levels (including hypertension and prehypertension) with reduced fecundability among young childbearing-age couples is not yet elucidated completely.

OBJECTIVE: The purpose of this study was to investigate the association between abnormal preconception blood pressure level and time to pregnancy among couples who are attempting to conceive their first pregnancy.

STUDY DESIGN: A total of 2,234,350 eligible couples (with no previous gravidity and whose female partners were 20—49 years old) participated in the National Free Preconception Check-up Projects from January 1, 2015, to December 31, 2016. Each couples' preconception blood pressure levels were measured, and time to pregnancy was recorded. Cox models for discrete survival time were used to estimate fecundability odds ratios and their corresponding 95% confidence intervals after adjustment for age, ethnicity, educational level, occupation, household registration, region, tobacco exposure, alcohol intake, body mass index, duration of marriage of the couples, and fasting plasma glucose levels of the female partner.

RESULTS: Compared with normotensive women, those women with hypertension (systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg) had a 21% lower pregnancy rate (fecundability odds ratio, 0.79; 95% confidence interval, 0.78—0.81). A similar finding was found among men (fecundability odds ratio, 0.89; 95% confidence interval, 0.88—0.90). Prehypertension (systolic blood pressure between 120 and 139 mm Hg, and/or a diastolic blood pressure between 80 and 89 mm Hg) in both male and female partners was associated slightly with reduced fecundability odds ratios. Compared with couples in which both partners were normotensive, the pregnancy rate was reduced by 27% (fecundability odds ratio, 0.73; 95% confidence interval, 0.69—0.77) among couples in which both partners had hypertension.

CONCLUSION: Abnormal preconception blood pressure levels were associated with prolonged time to pregnancy among couples who were attempting to conceive their first pregnancy; the mechanism is worth further investigation.

Key words: blood pressure, hypertension, preconception, pregnancy rate, time to pregnancy

Infertility remains a public health problem worldwide.[1] Although infertility is considered a non-life-threatening disease, it brings about overwhelming suffering, which has social, economic, psychologic, and physical effects on couples.[2,3] Zhou et al[4] reported that the prevalence of infertility among women who are attempting to conceive reaches 25% in China. Investigating infertility is a difficult task, not only because of the marked discrepancies in the comprehensive range of treatments, but also because of the difficulty in determining the appropriate timing of infertility.[5,6] In practice, time to pregnancy (TTP) is 1 of the most important and fundamental indices to evaluate couples' fecundability, and prolonged TTP can reflect the decline of couple's fecundability.[7,8] Couples who fail to achieve clinical pregnancy after ≥12 menstrual cycles with regular unprotected sexual intercourse are classified as subfecundity.[8] The increasing rate of subfecundity may be associated with the rising prevalence of certain chronic diseases, such as diabetes mellitus,[9] obesity,[10] and hypertension[11] among young adults.

Hypertension is 1 of the most common chronic diseases worldwide.[12] Recent data have shown that the prevalence of hypertension in young Chinese adults (aged 20—49 years) has reached 7.9—26.8% and is expected to increase until 2030.[13] Some studies demonstrated the association between numerous adverse pregnancy outcomes, including preterm birth, miscarriage and maternal hypertension.[14] Elevated blood pressures (BPs) are likely to accompany poor physical conditions, which results in decreased quality of male sperm or female oocyte[15,16]; the potential hazards on couples' fecundability are imperceptible but worth evaluating. Eisenberg et al[9] and Nobles et al[11] studied the possible effect of hypertension on couples' fecundity, but their samples were too small to draw significant conclusions. Only 16.0—39.3% of young adults were reported to be aware of their abnormal BP,[13] and approximately 50% of prehypertensive patients are likely to progress to hypertension in the following 10 years.[17] Therefore, BP monitoring routine among young couples who attempt to conceive is particularly important. To our knowledge, population evidence to verify the effect of abnormal BP (including prehypertension and hypertension) on TTP among young couples remains lacking.

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AJOG at a Glance

Why was this study conducted?

The increasing prevalence of subfertility has been a serious public health problem; thus, investigating the risk factors that affect fecundability is necessary.

Key findings

Among couples who attempt to conceive their first pregnancy, the women and men with hypertension have a 21% and 11% lower pregnancy rate, respectively, when compared with the normotensive ones.

What does this add to what is known?

Abnormal preconception blood pressure levels among couples who attempted to conceive their first pregnancy were associated with their reduced fecundability.

To eliminate the potential impacts of previous pregnancy outcomes and recent changes in China's 2-child family planning policy on couples' TTP, we chose couples who attempted to conceive their first pregnancy as the study population. These couples were preponderant among those who desired to have children. The data from the National Free Pre-conception Check-up Projects (NFPCP) were used to investigate the relationship between couples' abnormal preconception BP (including hypertension and prehypertension) and their TTP to provide adequate lifestyle management to couples who attempt to conceive.

Materials and Methods

Study population

From January 1, 2015 to December 31, 2016, 3,507,490 Chinese couples whose female partners were 20−49 years old without previous pregnancy participated in the NFPCP. All participants received free prepregnancy medical examinations and were followed for pregnancy outcome. More information about the government-supported project was previously reported.[18,19] Based on the exclusion criteria, 1,273,140 couples were not included for the following reasons: 245,721 couples had irregular menstrual cycles of their female partners; 13,575 couples confirmed pregnancy at the time of their participation; 141,655 couples were not planning for pregnancy immediately; 143,779 couples were not suitable for pregnancy at the time of their participation because of medical conditions; 664,151 couples were pregnant at the first menstrual cycle; and 64,259 couples were missing some key information (Figure 1). A total of 2,234,350 couples finally were included in the study. Notably, women who got pregnant at their first menstrual cycles after they participated in the NFPCP might have been pregnant during checkup but were unaware that they were. To ensure that all women were not pregnant when they joined the project and to reduce unplanned pregnancy bias, we included only couples whose female partners had at least 1 normal menstruation after taking part in the NFPCP. This study was approved by the Institutional Research Review Board at the National Health Commission and the National Health Council's Ethics Review Committee.

Exposure measurements

Experienced physicians measured BP from participant's right arm using an automatic sphygmomanometer after at least 10 minutes of rest. Based on the Joint National Committee 7 classification,[20] we defined normal BP as systolic BP (SBP) <120 mm Hg and diastolic BP (DBP) <80 mm Hg, prehypertension as SBP between 120 and 139 mm Hg and/or DBP between 80 and 89 mm Hg, and hypertension as SBP ≥140 mm Hg and/or DBP ≥90 mm Hg. These definitions are consistent with the standards for clinical diagnosis of hypertension in China.[21]

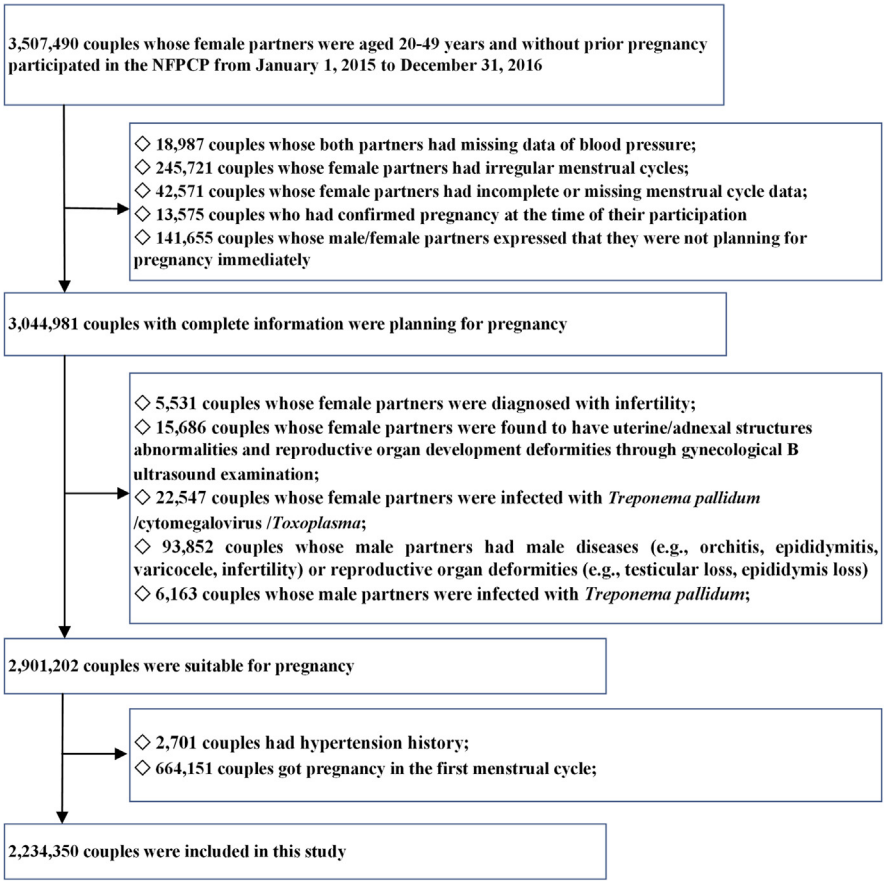
Ascertainment of outcomes

After obtaining the health examination evaluation report, couples were followed through telephone interviews by trained local health professionals every 3 months. Confirmed pregnancy was based on the hospital gynecologic B mode ultrasound examination result, which was self-reported by female partners. TTP in cycles was calculated with the use of the following formula: TTP=(date of last menstrual period [pregnant couples] or the most recent follow-up [unpregnant couples]−date of baseline questionnaire completion)/average menstrual cycle length+1. A woman's self-reported length of average menstrual cycle was based on the general menstruation situation in the recent 6 months. TTP was rounded to the nearest whole number. All couples were followed while attempting to conceive until they reported pregnancy or up to 1 year. TTP was considered censored if the female partner was lost to follow up, was not pregnant after 12 menstrual cycles, or at the end of 2017.

Ascertainment of covariates

Information on the participant's date of birth, ethnicity, educational level, occupation, household registration, marriage date, tobacco exposure, alcohol intake, and menstruation situation were collected from a unified questionnaire, which was conducted by trained local health professionals. Age was calculated with the use of the date of examination and birth; duration of marriage was the interval in months between the marriage date and the examination date. In this study, regular menstrual cycle was defined as a cycle with an intermenstrual interval of 21−35 days, and the variation of cycle length from 1 period to another was ≤7 days.[22] The bodyweight (nearest 0.1 kg) and height (nearest 0.1 cm) of the couples were measured by standardized techniques in a bright indoor environment with their coats, shoes, and accessories removed.[23] Body mass index (BMI) was calculated with the use of weight and height based on the following formula: BMI=weight/height^2 (kilograms/meter^2). BMI was categorized into 4 groups: underweight (<18.5 kg/m^2), normal weight (18.5−23.9 kg/m^2), overweight (24.0−27.9 kg/m^2), and obesity (≥28.0 kg/m^2).[24] The woman's

FIGURE 1
Flowchart of the study population



All the arrows pointing to the right indicate why and how many people were excluded for specific reasons.

NFPCP, National Free Pre-conception Check-up Projects.

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fasting plasma glucose level was categorized into 3 groups: normal (<6.1 mmol/L), impaired glucose tolerance (6.1−7.0 mmol/L), and diabetes mellitus (≥7.0 mmol/L).[25] According to their self-reported information, alcohol intake was divided into 2 categories: no drinking (no) or occasionally/frequently drinking (yes). Similarly, tobacco exposure was divided into 2 categories: active or passive smoker (yes) or no exposure (no). The inspection agencies were divided into 3 regions (Eastern/Central/Western) according to their location.[26]

Statistical analyses

All data were transferred into the NFPCP medical service information system for storage, and Microsoft SQL server 2012 (Microsoft Corporation, Redmond, WA) was used to manage and clean the data. Mean (standard deviation) and counts (percentages) were used to describe the baseline characteristics of participants. The cumulative pregnancy rates in each menstrual cycle were estimated with the Kaplan-Meier method (product-limit method). Cox models for discrete survival time were used to estimate fecundability odds ratios (FORs) and their corresponding 95% confidence intervals (CIs). FORs estimated the odds of becoming pregnant in the current cycle for participants with or without abnormal BP, conditional on not being pregnant in the previous cycle.[9] FOR <1 indicates a reduction in fecundability or a longer TTP, whereas FOR >1 indicates a shorter TTP. To examine the robustness of our findings, we used 2 models by adjusting for different covariates. Model A was adjusted for some demographic characteristics that included age (continuous), ethnicity (Han/others), educational level (high school or below/bachelor's degree or above), occupation (farmer/worker/civil servant/others), household registration (rural/urban), region (Eastern/Central/Western), and duration of marriage. Model B was adjusted additionally for some potential influential factors of fecundability based on model A and included tobacco exposure (yes/no), alcohol intake (yes/no), and BMI (underweight/normal/overweight/obesity). Female-specific model B was adjusted additionally for the fasting plasma glucose level (normal/impaired fasting plasma glucose/diabetes mellitus). Both models A and B were fitted by the female and male data separately and were refitted subsequently with all the female and male data to assess the couples' health and fecundity jointly. In sensitivity analysis, multiple imputation with a fully conditional specification method[27] was conducted to deal with missing data for all participants that was used at baseline; the imputation model included all predictors in the univariate analysis. The models were then rerun. Subgroup analysis was performed to compare the FORs among couples with different characteristics. All these analyses were carried out with the use of SAS software (version 9.3; SAS Institute, Inc, Cary, NC); Kaplan-Meier plot and heatmap were created with GraphPad Prism 7 (GraphPad Software, Inc, La Jolla, CA). Two-sided probability values of <.05 were deemed to be statistically significant.

Result

In this cohort, 2,234,350 couples were eligible for the study. The mean ages of female and male partners were 25.58 and 27.21 years, respectively. Most couples were Han Chinese and farmers and had an educational level of high school or below. More male partners reported that they had alcohol intake (23.78% vs 3.09%) and tobacco exposure (30.58% vs 9.36%) compared with female partners. The prevalence of prehypertension and hypertension in women were

TABLE 1
Baseline characteristics of the study population

Variables	Female	Male
Age, y[a]	25.58±3.53	27.21±3.92
<24, n (%)	883,174 (39.53)	512,079 (22.93)
25–29, n (%)	1,117,874 (50.03)	1,268,786 (56.82)
30–34, n (%)	180,673 (8.09)	342,663 (15.35)
35–39, n (%)	39,542 (1.77)	76,957 (3.45)
40–45, n (%)	11,018 (0.49)	25,298 (1.13)
>45, n (%)	2,069 (0.09)	8,567 (0.38)
Ethnicity, n (%)		
Han	2,015,038 (90.18)	2,020,591 (90.43)
Others	219,312 (9.82)	213,759 (9.57)
Educational level		
High school or below, n (%)	1,518,435 (70.81)	1,546,467 (72.01)
Bachelor's degree or above, n (%)	625,920 (29.20)	601,059 (27.99)
Missing, n	89,995	86,824
Occupation		
Farmer, n (%)	1,384,965 (64.89)	1,368,093 (64.08)
Worker, n (%)	179,192 (8.40)	245,323 (11.49)
Civil servant, n (%)	275,676 (12.92)	237,811 (11.14)
Others, n (%)	294,479 (13.80)	283,665 (13.29)
Missing, n	100,038	99,458
Household registration		
Rural, n (%)	1,952,606 (87.40)	1,918,619 (85.88)
Urban, n (%)	281,589 (12.60)	315,523 (14.12)
Missing, n	155	208
Region, n (%)		
Eastern	606,543 (27.15)	
Central	995,633 (44.56)	
Western	632,174 (28.29)	
Tobacco exposure		
Yes, n (%)	208,574 (9.36)	680,955 (30.58)
No, n (%)	2,018,989 (90.64)	1,546,041 (69.42)
Missing, n	6,787	7,354
Alcohol intake		
Yes, n (%)	68,657 (3.09)	528,947 (23.78)
No, n (%)	2,155,141 (96.91)	1,695,804 (76.22)
Missing, n	10,552	9,599

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24.75% and 1.26%, respectively, and those in men were 49.75% and 3.84%, respectively (Table 1). Notably, the prevalence of hypertension among the excluded couples because of pregnancy at the first menstrual cycle was lower than that among the included couples (Table S1).

At the end of 1-year follow up, 798,610 couples achieved pregnancy within 12 menstrual cycles, among which 56.60% were pregnant within 3 TTPs and 83.04% were pregnant within 6 TTPs. According to the Kaplan-Meier method, the cumulative pregnancy rate in 12 cycles was 41.95%. Female partners with hypertension (33.90%) or prehypertension (41.61%) had significantly lower pregnancy rate than those with normal BP (42.23%; Figure 2). As for male partners, no statistically significant difference was found in the cumulative pregnancy rate between prehypertensive and normotensive men (P=.161). However, a statistically significant difference was noted in the cumulative pregnancy rate between hypertensive and normotensive men (Figure 2).

In female- or male-specific models, fecundability continued to decline with higher BP levels when adjusted for potential factors (Table 2). Compared with normotensive women, those with hypertension had 21% lower pregnancy rate (FOR, 0.79; 95% CI, 0.78–0.81). A similar finding was demonstrated in men, but the effect on fecundability was milder (FOR, 0.89; 95% CI, 0.88–0.90). The FORs in either men or women with prehypertension were all close to 1.0 yet still yielded a statistical significance.

In the couple-based models, the pregnancy rate was reduced by 27% (FOR, 0.73; 95% CI, 0.69–0.77) if both partners had hypertension. This rate was even lower than that if only 1 partner had hypertension (only female with hypertension: FOR, 0.81; 95% CI, 0.77–0.85; only male with hypertension: FOR, 0.94; 95% CI, 0.92–0.95; Figure 3). The interaction between female and male partners' BP status was statistically significant (P<.001). The pregnancy rate was slightly increased in couples whose male partner had normal BP and female partner had prehypertension (FOR, 1.04; 95% CI, 1.03–1.05).

With implementation of multiple imputation, the results from either female or male models were not altered (FORs, 0.79 [95% CI, 0.74–0.81] and 0.99 [95% CI, 0.98–0.99] in women and

TABLE 1
Baseline characteristics of the study population *(continued)*

Variables	Female	Male
Body mass index, kg/m^2		
Underweight (<18.5), n (%)	365,106 (16.42)	100,658 (4.52)
Normal (18.5–23.9), n (%)	1,602,475 (72.07)	1,441,970 (64.78)
Overweight (24.0–27.9), n (%)	206,439 (9.28)	548,899 (24.66)
Obesity (≥28.0), n (%)	49,354 (2.22)	134,464 (6.04)
Missing, n	10,976	8,359
Duration of marriage, month[b]	1 (0-6)	1 (0-6)
Missing, n	253,254	
Fasting plasma glucose level, n (%)		
Normal (<6.1 mmol/L)	2,127,082 (95.89)	—
Impaired glucose tolerance (6.1–6.9 mmol/L)	65,275 (2.94)	—
Diabetes mellitus (≥7.0 mmol/L)	25,979 (1.17)	—
Blood pressure level		
Normal, n (%)	1,649,183 (73.99)	1,034,483 (46.40)
Prehypertension, n (%)	551,736 (24.75)	1,109,228 (49.75)
Hypertension, n (%)	28,117 (1.26)	85,719 (3.84)
Missing, n	5,314	4,920

[a] Data are given as mean±standard deviation; [b] Data are given as median (interquartile range).
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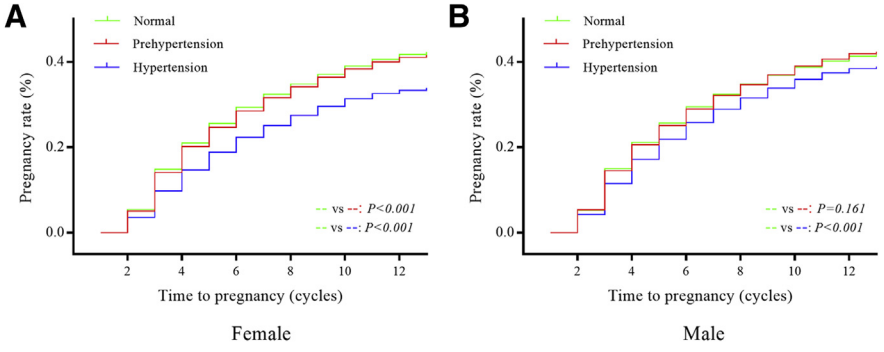
0.90 [95% CI, 0.89–0.91] and 0.99 [95% CI, 0.98–0.99] in men, respectively, for the hypertension and prehypertension groups compared with the normal BP group). In subgroup analysis, most FORs of hypertension remained significant, but those of prehypertension were not significant in some subgroups, such as in ages <24 and 45–49 years, non-Han ethnicity, civil servant, and tobacco exposure (Table S2). As a secondary analysis, we used the American Heart Association standard[28] to explore the association, and the results still indicated that abnormal BP (SBP, ≥120 mm Hg, or DBP ≥80 mm Hg) was associated with prolonged TTP, but the effects were weaker (Table S3). Under this stricter standard, the FORs of hypertension (SBP, ≥130 mm Hg, or DBP, ≥80 mm Hg) and elevated BP (≤120 mm Hg; SBP, <130 mm Hg, and DBP <80 mm Hg) were similar.

FIGURE 2
Kaplan-Meier plot of pregnancy rates for different blood pressure levels



A, Female; **B,** Male. Probability values were calculated with the log-rank test.
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Comment

To our knowledge, this is the first large-scale population-based epidemiologic study on the fecundability of prepregnancy couples with hypertension or prehypertension in China. The findings of this study suggested that abnormal BP in either partner of the couple before conception was associated prospectively with a reduction of fecundability. We observed that the pregnancy rate was reduced by 27% if couples were both hypertensive. The effect of prehypertension was relatively weaker but was still statistically significant.

Our study data were obtained from a nationwide register-based cohort; the prevalence of hypertension were 1.26% and 3.84% for women and men, respectively, which were lower than those obtained by other studies.[13] The inconsistent results were due to the inclusion of only couples with no previous gravidity in the present study; thus, most were likely young couples with low prevalence of chronic disease. In our study, most couples who had hypertension or prehypertension were unaware of their abnormal BP status before physical examinations. Our result highlighted the importance of early screening and management for hypertension, particularly among prepregnant reproductive-age couples.

Some population-based studies have been conducted to elucidate the impairing effect of hypertension on fecundity, but the results were inconsistent. Eisenberg et al[9] used the Longitudinal Investigation of Fertility and the Environment Study data to explore the association of men and women with diabetes mellitus and other factors that included hypertension with TTP, but the effects of high BP on TTP were not statistically significant because of small sample size (501 couples). Nobles et al[11] evaluated women with history of

TABLE 2
Abnormal blood pressure and fecundability odds ratios based on female or male model

Group	Fecundability odds ratios (95% confidence interval)		
	Crude	Model A[a]	Model B[b]
Female			
Hypertension	0.74 (0.72–0.76)	0.77 (0.75–0.79)	0.79 (0.78–0.81)
Prehypertension	0.97 (0.97–0.98)	0.99 (0.98–0.99)	0.99 (0.98–0.99)
Normal	Reference	Reference	Reference
Male			
Hypertension	0.88 (0.87–0.89)	0.90 (0.89–0.92)	0.89 (0.88–0.90)
Prehypertension	1.00 (0.99–1.01)	0.99 (0.98–0.99)	0.99 (0.98–0.99)
Normal	Reference	Reference	Reference

[a] Adjusted for age (continuous), ethnicity (Han/others), educational level (high school or below/bachelor's degree or above), occupation (farmer/worker/civil servant/others), household registration (rural/urban), region (eastern/central/western), and duration of marriage; [b] Additionally adjusted for tobacco exposure (yes/no), alcohol intake (yes/no), and body mass index (underweight/normal/overweight/obesity) based on model A; female individual model B was additionally adjusted for the fasting plasma glucose level (normal/impaired fasting plasma glucose/diabetes mellitus).

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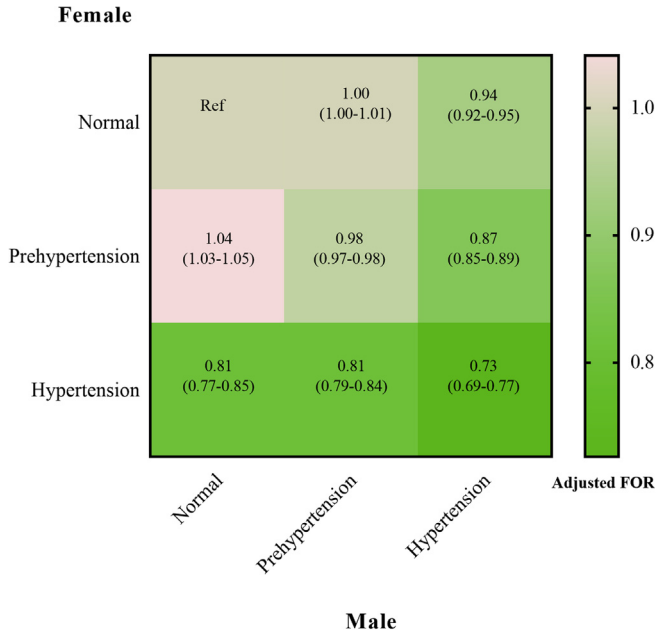
pregnancy loss and who were attempting to conceive and found a negative association between preconception BP and fecundability. Given that previous adverse pregnancy outcomes are likely to be an important factor that affects fecundability,[29] the results of Nobles et al could not be extrapolated to couples in general population. Therefore, we included only women without pregnancy history and reproductive organ malformation, which was confirmed by B ultrasound examination when they participated in the project.

The potential impairment mechanism of hypertension on male fecundability might be due to sperm damage. Population-based studies showed that men with hypertension have lower semen volume, sperm motility, total sperm count, and motile sperm count compared with normotensive men.[30,31] The underlying mechanism might be that hypertension affects the capillaries of the testis, which leads to reduced testosterone levels.[15,32] Meanwhile, semen quality is regarded as an aggregate proxy for the somatic health of men.[33,34] As a common chronic disease, hypertension is often associated with weaker immunity, chronic inflammatory response, and other subhealth status.[35] However, whether this association is the pathogeny of semen quality damage is not clear.[30] A rat model demonstrated that enalapril treatment partially protects testicular alterations that are caused by abnormal BP and restores normal spermatozoa production.[36]

Because human oocyte quality is difficult to assess directly, only some mouse model studies showed that hypertension is associated with reduced oocyte numbers, sexual behavior, and luteinization of hormone levels.[16] However, the exact mechanism and etiologic pathway are unclear. Notably, polycystic ovary syndrome is a condition directly associated with obesity, insulin resistance, and metabolic syndrome; hypertension is 1 of the typical symptoms of metabolic syndrome.[37,38] As 1 of the most common causes of female infertility, whether polycystic ovary syndrome plays a mediating role between hypertension and infertility deserves further study. Although we excluded women who might have polycystic ovary syndrome by ultrasound scanning, the underlying pathologic and physiologic changes were not observed easily. These dynamic changes might influence the interpretation of fecundability.

Our study findings were strengthened by the large population-based sampling framework rather than reliance on a convenient or clinically based sample, and the prospective assessment of fecundability was performed under uniform standards. However, although this was a prospective study, we were unable to confirm whether the association between preconception BP and subfecundity was causality. The United States claims data showed that men who were diagnosed with infertility have a significantly higher risk of adverse health outcomes, including hypertension, in the years after an infertility evaluation,[39] which indicates that hypertension/prehypertension and infertility may coexist, whichever was diagnosed first would be regarded as the cause. More community intervention trials should be implemented to verify the causality. Additionally, we did not record the exact number of each female's menstrual cycle; instead, we calculated an estimated cycle count through the couple's actual waiting days of pregnancy divided by the average menstrual cycle length. Although this is a common approach to obtain TTP,[40] misclassification bias could not be avoided, particularly among women with irregular menstruation, which would lead to bias results towards the null and underestimate the true association. Meanwhile, a considerable limitation was that the diagnosis of hypertension and prehypertension was based only on the participant's single BP measurement in resting state and not on multiple BP measurements. We were also unable to obtain the follow-up medical records for participants with a single abnormal BP. However, some research papers that used the NFPCP data showed that single resting BP data could also show the basic situation of hypertension and prehypertension of reproductive-age Chinese couples to some extent.[41,42] In addition, although many studies reported that antihypertensive drugs potentially can affect sperm quantity and quality,[37] we did not collect data on the use of antihypertensive drugs among couples. Finally, the findings should be extrapolated cautiously to

FIGURE 3
Heatmap for abnormal blood pressure and fecundability odds ratios based on the couple model



Fecundability odds ratios were adjusted for both partners' age (continuous), ethnicity (Han/others), educational level (high school or below/bachelor's degree or above), occupation (farmer/worker/civil servant/others), household registration (rural/urban), region (eastern/central/western), duration of marriage, tobacco exposure (yes/no), alcohol intake (yes/no), body mass index (underweight/normal/overweight/obesity), and female partner's fasting plasma glucose level (normal/impaired fasting plasma glucose/diabetes mellitus).

FOR, fecundability odds ratio; *Ref*, reference.

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general population decision-making and fertility guidance, because our study population did not include couples with pregnancy history.

We found evidence of the association between abnormal preconception BP and longer TTP among couples who were attempting to conceive their first pregnancy in China, and the mechanism is worth further investigation. The finding has public health significance and practical value. ■

Acknowledgments

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Author and article information

From the Key Laboratory of Environmental Medicine and Engineering of Ministry of Education, Department of Epidemiology and Statistics, School of Public Health, Southeast University, Nanjing, Jiangsu, China (Drs Hong, Xuan, B. Wang, and Ms. Huang); the National Research Institute for Family Planning (Dr Zhao, Ms. Dai, Qi, Yang, Y. Zhang, Mr. H. Zhang and Ma); the National Human Genetic Resources Center (Dr Zhao, Ms. Dai, Qi, Yang, Mr. H. Zhang and Ma); the Department of Maternal and Child Health, National Health Commission of the People's Republic of China (Dr Q. Wang, Shen, Xu, Y.P. Zhang and Yan) and the Graduate School of Peking Union Medical College, Beijing, China (Ms. Y. Zhang, and Mr. Ma); the Department of Epidemiology and Biostatistics, College of Public Health, Temple University, Philadelphia, PA (Dr Wu); the Mount Sinai Health System, New York, NY (Dr Fang).

[1]These authors contributed equally to this article.

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Corresponding author: Bei Wang, PhD. wangbeilxb@163.com; Xu Ma, MS. genetic88@126.com

TABLE S1
Blood pressure status of male and female partners among the included and excluded couples because of pregnancy at the first menstrual cycle

Blood pressure status	Hypertension, n (%)	Prehypertension, n (%)	Normal, n (%)	*P* values[a]
Female partners				
Included couples (n=2,234,350)	28,117 (1.26)	551,736 (24.75)	1,649,183 (73.99)	—
Excluded couples because of pregnancy in the first menstrual cycle (n=664,151)	5,524 (0.83)	135,797 (20.49)	521,305 (78.67)	<.001
Male partners				
Included couples (n=2,234,350)	85,719 (3.84)	1,109,228 (49.75)	1,034,483 (46.40)	—
Excluded couples because of pregnant in the first menstrual cycle (n=664,151)	17,508 (2.64)	304,274 (45.90)	341,125 (51.46)	<.001

[a] Comparison to the "included couples" by chi-square test.

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TABLE S2
Subgroup analysis for abnormal blood pressure and fecundability odds ratios and 95% confidence intervals based on female or male model

	Female		Male	
Variable	Prehypertension	Hypertension	Prehypertension	Hypertension
Age, y				
≤24	0.99 (0.99–1.01)	0.78 (0.75–0.81)	1.00 (0.99–1.01)	0.89 (0.86–0.91)
25–29	0.99 (0.98–1.00)	0.82 (0.79–0.84)	0.99 (0.98–0.99)	0.89 (0.88–0.91)
30–34	0.96 (0.94–0.98)	0.74 (0.68–0.80)	0.98 (0.96–0.99)	0.89 (0.86–0.92)
35–39	0.90 (0.86–0.95)	0.74 (0.62–0.88)	0.96 (0.93–0.99)	0.86 (0.80–0.93)
40–44	0.84 (0.74–0.95)	0.59 (0.42–0.84)	0.94 (0.88–1.01)	0.68 (0.59–0.80)
45–49	0.85 (0.55–1.31)	0.71 (0.26–1.98)	1.01 (0.88–1.15)	0.72 (0.55–0.95)
Ethnicity				
Han	0.99 (0.98–0.99)	0.79 (0.77–0.81)	0.99 (0.98–0.99)	0.89 (0.88–0.90)
Others	1.01 (0.98–1.03)	0.83 (0.76–0.91)	1.01 (0.99–1.03)	0.96 (0.90–1.01)
Educational level				
High school or below	0.98 (0.98–0.99)	0.75 (0.72–0.77)	0.98 (0.98–0.99)	0.85 (0.84–0.87)
Bachelor degree or above	1.02 (1.01–1.03)	0.91 (0.87–0.95)	1.01 (0.99–1.02)	0.97 (0.95–0.99)
Occupation				
Farmer	0.97 (0.97–0.98)	0.72 (0.70–0.74)	0.98 (0.97–0.99)	0.82 (0.80–0.83)
Worker	1.01 (0.99–1.03)	0.88 (0.81–0.95)	1.03 (1.01–1.04)	0.98 (0.94–1.01)
Civil servant	1.01 (0.99–1.03)	0.94 (0.88–0.99)	1.01 (0.99–1.03)	0.98 (0.94–1.01)
Others	1.03 (1.01–1.05)	0.93 (0.88–0.99)	0.99 (0.97–1.00)	0.97 (0.93–0.99)
Household registration				
Rural	0.99 (0.98–0.99)	0.78 (0.76–0.80)	0.99 (0.98–0.99)	0.87 (0.86–0.89)
Urban	1.01 (0.99–1.03)	0.92 (0.86–0.98)	0.99 (0.97–1.00)	0.98 (0.95–1.01)

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(continued)

TABLE S2
Subgroup analysis for abnormal blood pressure and fecundability odds ratios and 95% confidence intervals based on female or male model *(continued)*

	Female		Male	
Variable	Prehypertension	Hypertension	Prehypertension	Hypertension
Region				
Eastern	1.03 (1.01–1.04)	0.89 (0.86–0.93)	1.04 (1.02–1.05)	0.96 (0.94–0.99)
Central	0.97 (0.96–0.98)	0.68 (0.66–0.71)	0.99 (0.98–0.99)	0.81 (0.79–0.82)
Western	1.01 (0.99–1.02)	0.92 (0.88–0.97)	0.95 (0.94–0.96)	0.96 (0.93–0.99)
Tobacco exposure				
Yes	1.02 (0.99–1.03)	0.91 (0.85–0.97)	1.01 (0.99–1.02)	0.95 (0.93–0.97)
No	0.99 (0.98–0.99)	0.78 (0.76–0.80)	0.98 (0.98–0.99)	0.86 (0.84–0.87)
Alcohol intake				
Yes	1.01 (0.97–1.04)	0.98 (0.87–1.10)	0.99 (0.98–0.99)	0.98 (0.95–0.99)
No	0.99 (0.98–0.99)	0.78 (0.77–0.80)	1.00 (0.99–1.01)	0.85 (0.84–0.87)
Body mass index, kg/m^2				
Underweight (<18.5)	1.02 (1.00–1.03)	0.92 (0.86–0.98)	0.97 (0.94–0.99)	0.91 (0.84–0.99)
Normal (18.5–23.9)	1.01 (0.99–1.01)	0.84 (0.81–0.86)	0.99 (0.99–0.99)	0.91 (0.90–0.93)
Overweight (24.0–27.9)	0.91 (0.89–0.92)	0.72 (0.68–0.76)	0.99 (0.98–1.00)	0.88 (0.86–0.90)
Obesity (≥28.0)	0.84 (0.81–0.86)	0.52 (0.47–0.56)	0.96 (0.94–0.98)	0.85 (0.82–0.88)
Fasting plasma glucose level, mmol/L				
Normal (<6.1)	0.98 (0.97–0.98)	0.79 (0.77–0.81)	—	—
Impaired glucose tolerance (6.1–6.9)	0.98 (0.95–1.02)	0.79 (0.70–0.89)	—	—
Diabetes mellitus (≥7.0)	1.05 (0.99–1.12)	0.68 (0.56–0.82)	—	—

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TABLE S3
Abnormal blood pressure and fecundability odds ratios and 95% confidence intervals based on the 2017 American Heart Association standard

Group	Crude fecundability odds ratios	Model A[a]	Model B[b]
Female			
Hypertension	0.96 (0.96–0.97)	0.97 (0.97–0.98)	0.98 (0.97–0.98)
Elevated blood pressure	0.96 (0.95–0.97)	0.99 (0.98–0.99)	0.99 (0.98–0.99)
Normal	Reference	Reference	Reference
Male			
Hypertension	0.99 (0.98–0.99)	0.99 (0.98–0.99)	0.98 (0.98–0.99)
Elevated blood pressure	0.99 (0.99–1.00)	0.99 (0.98–0.99)	0.98 (0.98–0.99)
Normal	Reference	Reference	Reference

Note: Elevated blood pressure was defined as systolic blood pressure between 120–129 mm Hg and diastolic blood pressure <80 mm Hg; hypertension was defined as systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg.

[a] Adjusted for age (continuous), ethnicity (Han/others), educational level (high school or below/bachelor degree or above), occupation (farmer/worker/civil servant/others), household registration (rural/urban), region (eastern/central/western) and duration of marriage; [b] Additionally adjusted for tobacco exposure (yes/no), alcohol exposure (yes/no), and body mass index (underweight/normal/overweight/obesity) based on model A; female individual model B was additionally adjusted for the fasting plasma level (normal/impaired fasting glucose/diabetes mellitus).

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