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Summary: The prevalence of hypertensive disorders in China was much higher than that in the United States. Considering the large population with wide geographic area of China, we aimed to add more information regarding the risk factors for hypertensive disorders of pregnancy. A case-control study was performed on 373 hypertensive cases and 507 normotensive controls. Participants were recruited from 2008 to 2014 in Yichang Maternal and Child Health Care Center in Hubei province and Anyang Maternal and Child Health Care Hospital in Henan province, China. Socio-demographic factors, family-related factors, pregnancy-associated factors, factors related to daily life behaviors and psychosocial factors were investigated with respect to hypertensive disorders in pregnancy through well-designed questionnaire. Chi-square test, t-test, univariate logistic regression analysis, and multivariate logistic regression analysis were used to find the possible risk factors behind hypertensive disorders in pregnancy. The results showed that family history of cardiovascular diseases (OR=6.18, 95% CI, 2.37 to 16.14), history of pregnancy-induced hypertension (OR=16.64, 95% CI, 5.74 to 48.22), low maternal educational level (OR=2.81, 95% CI, 1.30 to 6.04), and poor relationship with their parents-in-law (OR=3.44, 95% CI, 1.55 to 7.59) had statistically significant associations with hypertensive disorders in pregnancy through multivariate logistic regression analysis. Increased maternal age, increased pre-pregnancy body mass index, living in rural area, low paternal education level, family history of hypertension, passive smoking one year before and/or in pregnancy, and poor sleeping quality were significantly associated with hypertensive disorders in pregnancy from univariate logistic regression analysis while the associations became uncertain when they were entered for multivariate logistic regression analysis. It was concluded that family history of cardiovascular diseases, history of pregnancy-induced hypertension, low maternal educational level, and poor relationship with their parents-in-law were independent risk factors for hypertensive disorders among Chinese pregnant women.

Key words: risk factors; hypertensive disorders; pregnancy

Hypertensive disorders in pregnancy, also referred to as pregnancy-induced hypertension include chronic hypertension, gestational hypertension, preeclamspsia/eclampsia, and preeclampsia superimposed on chronic hypertension, and occur in 6%–8% of pregnancies in the United States and are major causes of maternal and neonatal mortality and morbidity^[1]. The incidence of hypertensive disorders in pregnancy in China is much higher than that in the United State, which is 9.4% according to a national epidemiological investigation in 1991^[2]. Another large population-based survey in 2005 revealed that the overall incidence rate of pregnancy-induced hypertension was 11.1% in Jiaxing area of Zhejiang province of China^[3]. It was reported that pregnancy-induced hypertension accounts for 15.7% of maternal deaths in the United States^[4]. A systematic review on a worldwide basis reported that hypertensive disorders account for 9.1% of maternal morbidity in Asia^[5].

In fact, hypertensive disorders in pregnancy can do much harm both for mother and newborns during perinatal period. Expectant mothers with hypertensive disorders are prone to develop potentially lethal complications, such as acute renal failure, acute heart failure and disseminated intravascular coagulation^[1, 6]. Moreover, the incidence of complications in severe pregnancy-induced hypertension was significantly higher than that in mild to moderate pregnancy-induced hypertension^[6]. Fetus with hypertensive mother is predisposed toward the development of adverse complications, such as placental abruption, intrauterine growth restriction, premature delivery, and even intrauterine fetal death^[7–9]. The prevention and control of hypertensive disorders in pregnancy are of great importance in improving maternal and fetal health.

However, the causes of most cases of hypertensive disorders in pregnancy remain poorly understood. Multiple risk factors have been described including pater-

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nal-related risk factors such as limited sperm exposure^[10]. maternal-specific risk factors such as increasing maternal age^[11] and family history of hypertension^[12], and pregnancy-associated risk factors such as multiple pregnancy^[9]. Despite the researches of the many risk factors for hypertensive disorders in pregnancy before, the previous studies were mainly conducted in western countries. The situation in China, a developing country with the world's largest population dispersed in wide geographical areas remains to be elucidated. According to a 2011 meta-analysis on the risk factors of hypertensive disorders, only 9 studies with a total of $160\overline{8}$ cases and 32 416 controls were eligible, most of which came from North, Northwest, Central South, South and Southeast of China^[13]. More evidence on the risk factors of hypertensive disorders is needed to be discovered.

The study was conducted in Hubei and Henan province, located in Central South and Central East of China respectively, which we thought would add new evidence on the risk factors of hypertensive disorders in pregnancy considering the new study site. The study is part of our research on the association between renin-angiotensin system gene polymorphisms of mothers and fetus and the risk of pregnancy-induced hypertension. It aims to find the risk factors for hypertensive disorders in pregnancy and the strength of risk imposed by the risk factors, thus providing basis for further investigation of its genetic background.

1 MATERIALS AND METHODS

1.1 Ethics Committee Approval

The study has been ethically approved by the Institutional Review Board of Tongji Medical College, Huazhong University of Science and Technology, China. **1.2 Study Participants**

A case-control study was conducted on 373 Chinese pregnant women with hypertensive disorders and 507 normotensive control subjects. From 2008 to 2014, we recruited subjects from Yichang Maternal and Child Health Care Center in Hubei province and Anyang Maternal and Child Health Care Hospital in Henan province, China. The diagnostic criteria for hypertensive disorders in pregnancy were referred to the disease identification code in "Chinese Obstetrics and Gynecology"^[14]. Pregnant women with history of hypertension, diabetes mellitus, cardiovascular diseases, renal diseases and other pregnancy-associated complications were excluded. All study participants were recruited at their first diagnosis on prenatal care.

1.3 Data Collection

A questionnaire with five dimensions was designed after literature review and experts appraisal. To ensure the data quality, we trained the head nurses in the two hospitals on how to collect data and then the head nurses trained their on-duty nurses before data collection. Besides, we collected the questionnaires and conducted the data entry every two months, so that timely feedback could be conveyed to nurses to improve the accuracy and completeness of data collection continuously. All participants were invited to complete the questionnaire on a voluntary basis at their first diagnosis on prenatal care and they filled out the questionnaire under the guidance of the trained nurses. Informed consents were obtained before they filled out the questionnaire. The detailed five dimensions with corresponding specific terms were presented below:

(1) Socio-demographic factors: maternal age, maternal ethnicity, place of residence, maternal and paternal education level, maternal and paternal occupation;

(2) Family-related factors: history of pregnancy-induced hypertension of her mother and her mother-in-law, history of hypertension of her mother/brother/sister and mother-/brother-/sister-in-law, history of hypertension of her husband, history of diabetes of her mother/brother/sister, history of cardiovascular diseases of her mother/brother/sister;

(3) Pregnancy-related factors: pre-pregnancy body mass index, fetus number, parity, history of previous pregnancy-induced hypertension, chronic diseases before pregnancy, infectious disease during pregnancy, genital disease during pregnancy;

(4) Daily life behaviors: active smoking during pregnancy and one year before pregnancy, passive smoking during pregnancy and one year before pregnancy brought by her husband, alcohol drinking before pregnancy, sleeping quality during pregnancy, working status during pregnancy;

(5) Psychosocial factors: experience of anxiety during pregnancy, relationship with parents-in-law, occurrence of major stressful events in pregnancy (i.e. parents and/or brother/sister were in serious illness or died during pregnancy), severe dispute with husband in pregnancy.

1.4 Statistical Methods

Chi-square test and student *t*-test were used to compare the difference of risk factors distributed in hypertensive cases and normotensive controls depending on the type of data. Univariate logistic regression analysis was used to find the possible risk factors behind hypertensive disorders in pregnancy. Multivariate logistic regression analysis (backward stepwise method using maximum likelihood ratio approximation) was used to find the independent risk factors. *P* value less than 0.05 was considered to have statistical significance. All statistical analyses were realized through SPSS, version 21 (SPSS. Inc., USA).

Chi-square test was performed for all possible risk factors, and univariate logistic regression analysis was only performed for risk factors that had statistical significance in Chi-square test. Then multivariate logistic regression analysis was performed in factors that were also statistically significant in univariate logistic regression analysis. The results of both univariate and multivariate logistic regression analysis were presented in odds ratio (OR) with 95% confidence interval (CI).

2 RESULTS

In total, 373 hypertensive cases and 507 normotensive controls were recruited into our study. They were predominantly Chinese Han population participating in the research (98.4% in case group vs. 96.8% in control group). There was a statistically significant difference in term of distribution of age between case group and control group ($P \le 0.001$), and the majority of them were at the age between 20 to 30 years (53.5% in case group vs. 66.9% in control group). The detailed results of Chi-square test and univariate analysis for socio-demographic factors, family-related factors, pregnancy-related factors, factors related to daily life behaviors and psychosocial factors are shown respectively in tables 1-5. The results of multivariate logistic regression analysis are presented in table 6.

	Chi-squa	Chi-square test			
Factors	Case	Control	P value	Univariate analysis [*]	P value
	(<i>n</i> =373)	(<i>n</i> =507)			
Maternal age (years)					
≤19	9 (2.4%)	11 (2.2%)	< 0.001	1.39 (0.57, 3.41)	0.474
20≤ age <30	198 (53.5%)	336 (66.9%)		Reference	
30≤ age <35	93 (25.1%)	104 (20.7%)		1.52 (1.09, 2.11)	0.013
≥35	70 (18.9%)	51 (10.2%)		2.33 (1.56, 3.48)	< 0.001
Ethnicity					
Han	362 (98.4%)	485 (96.8%)	0.147	_	_
Others	6 (1.6%)	16 (3.2%)		_	_
Place of residence					
Rural area	123 (34.1%)	266 (53.8%)	< 0.001	2.26 (1.71, 2.99)	< 0.001
Urban area	238 (65.9%)	228 (46.2%)		Reference	
Maternal educational level					
Secondary and below	239 (65.8%)	206 (41.3%)	< 0.001	2.74 (2.07,3.63)	< 0.001
High and above	124 (34.2%)	293 (58.7%)		Reference	
Paternal educational level					
Secondary and below	230 (62.8%)	191 (38.1%)	< 0.001	2.75 (2.08, 3.63)	< 0.001
High and above	136 (37.2%)	310 (61.9%)		Reference	
Maternal occupation					
Occupied	305 (82.4%)	357 (72.7%)	0.001	1.76 (1.26, 2.46)	0.001
Non-occupied	65 (17.6%)	134 (27.3%)		Reference	
Paternal occupation					
Occupied	330 (90.9%)	441 (90.4%)	0.789	_	—
Non-occupied	33 (9.1%)	47 (9.6%)		—	_

Table 1 Distribution of socio-demographic factors between	en hypertensive cases and normotensive control subjects and
crude estimation of their associations	

^{*}Univariate analysis was used when the P value of Chi-square test was less than 0.05. The results were presented as OR with 95% CI.

As shown in table 1, maternal age greater than 35 years, living in rural areas, low maternal educational level, low paternal educational level, and maternal occupation status (occupied) were found in a higher proportion of pregnant women with hypertensive disorders than normotensive pregnant women. And the univariate logistic regression analysis showed that each of these factors imposed one to two more times risk of having hypertensive disorders for women in pregnancy.

The results of statistical analyses for family-related factors are seen in table 2. Only history of hypertension of her mother/brother/sister and history of cardiovascular disease of her mother/brother/sister were significantly different between hypertensive cases and normotensive controls. The univaritate logistic analysis showed history of hypertension of her mother/brother/sister and history of cardiovascular disease of her mother/brother/sister were significantly associated with hypertensive disorders in pregnancy.

Table 3 summarized the statistical results for pregnancy-related factors. Lightweight, overweight and obese before pregnancy, and history of previous pregnancy-induced hypertension were found in a higher percentage of women with hypertensive disorders than normotensive pregnant women. The univariate logistic regression analysis revealed that overweight, obesity before pregnancy and previous history of pregnancy-induced hypertension were risk factors while lightweight was a protective factor.

Table 4 presented the statistical results for daily life factors. Both active smoking before and in pregnancy were evenly distributed in hypertensive cases and normotensive controls while both passive smoking one year before and in pregnancy were not. Sleeping quality in pregnancy was also unevenly distributed between hypertensive cases and normotensive controls. Both alcohol drinking before and in pregnancy were scarce in both hypertensive cases and normotensive controls, and there was no statistically significant difference (14.0% vs. 13.8%, P=0.939; and 2.5% vs. 1.2%, P=0.158, respectively). Most of pregnant women still worked during pregnancy, and there was no difference between hypertensive cases and normotensive controls (71.3% vs. 65.0%, P=0.049). The univariate logistic regression analysis showed that passive smoking before and in pregnancy, and poor sleeping quality were statistically and significantly associated with hypertensive disorders in pregnancy.

Table 5 depicted the statistical results for psychosocial factors. More cases had an experience of anxiety during pregnancy (31.2% vs. 20.4%, P<0.001), and got along with their parents-in-law in a tense (38.1% vs. 16.6%, P<0.001) than normotensive controls. The occurrence of major stressful events and severe dispute with their husband were evenly distributed in hypertensive cases and normotensive controls. The univariate logistic regression analysis revealed that experience of anxiety in pregnancy and poor relationship with their parents-in-law were statistically associated with hypertensive disorders in pregnant women.

Factors	Chi-square test		D voluo	Universite enclusis*	D volue	
ractors —	Case (<i>n</i> =373)	Control (n=507)	<i>r</i> value	Univariate analysis	r value	
History of pregnancy-induced						
hypertension of her mother						
Yes	16 (5.7%)	12 (2.8%)	0.050	2.11 (0.98, 4.54)	0.055	
No	265 (94.3%)	420 (92.7%)		Reference		
History of hypertension of her mother/brother/sister						
Yes	101 (30.2%)	92 (29.8%)	0.001	1.75 (1.27, 2.43)	0.001	
No	233 (69.8%)	372 (80.2%)		Reference		
History of hypertension of her hus-						
band						
Yes	8 (2.3%)	13 (2.7%)	0.725	_	_	
No	343 (97.7%)	475 (97.3%)		_	—	
History of pregnancy-induced hy-						
pertension of her mother-in-law						
Yes	13 (4.5%)	13 (3.1%)	0.335	_	_	
No	276 (95.5%)	405 (96.9%)		_	_	
History of hypertension of her						
mother-/brother-/sister-in-law						
Yes	72 (21.2%)	84 (18.2%)	0.297	_	_	
No	268 (78.8%)	377 (81.8%)		_	_	
History of diabetes of her						
mother/brother/sister						
Yes	20 (5.8%)	26 (5.4%)	0.818	_	_	
No	324 (94.2%)	452 (94.6%)		_	_	
History of cardiovascular diseases of						
her mother/brother/sister						
Yes	58 (17.6%)	36 (8.1%)	< 0.001	2.42 (1.56, 3.77)	< 0.001	
No	272 (82.4%)	409 (91.9%)		Reference		

 Table 2 Distribution of family-related factors between hypertensive cases and normotensive control subjects and crude estimation of their associations

*Univariate analysis was used when the P value of Chi-square test was less than 0.05. The results were presented as OR with 95% CI.

Table 3 Distribution of pregnancy-related factors between hypertensive cases and normotensive control subjects and crude estimation of their associations

Factors	Chi-square test		P value	Univariate analysis [*]	P value
Tactors	Case (<i>n</i> =373)	Control (n=507)	1 value	Univariate analysis	<i>I</i> value
Pre-pregnancy body mass index					
(kg/m^2)					
Lightweight (<18.5)	25 (7.7%)	85 (18.9%)	< 0.001	0.44 (0.27, 0.71)	< 0.001
Normal weight (18.5–23.9)	196 (60.3%)	292 (65.0%)		Reference	
Overweight (24.0–27.9)	74 (22.8%)	56 (12.5%)		1.97 (1.33, 2.91)	< 0.001
Obesity (≥ 28.0)	30 (9.2%)	16 (3.6%)		2.79 (1.48, 5.26)	< 0.001
Fetus number					
One	340 (97.7%)	489 (98.0%)	0.770	_	_
Two/multiple	8 (2.3%)	10 (2.0%)		_	_
Parity					
Nullipatiry	149 (40.9%)	219 (43.9%)	0.386	_	_
Multiparity	215 (59.1%)	280 (56.1%)		_	_
History of previous preg-					
nancy-induced hypertension					
Yes	59 (32.8%)	7 (3.3%)	< 0.001	14.28 (6.32, 32.26)	< 0.001
No	121 (67.2%)	205 (96.7%)		Reference	
Chronic disease before pregnancy					
Yes	9 (2.8%)	5 (1.1%)	0.078	_	_
No	318 (97.2%)	460 (98.9%)		_	_
Infectious disease during pregnancy					
Yes	3 (0.9%)	14 (3.0%)	0.087	_	_
No	320 (99.1%)	455 (97.0%)		_	_
Genital disease during pregnancy					
Yes	4 (1.2%)	11 (2.3%)	0.394	_	_
No	318 (98.8%)	458 (97.7%)		_	_
Oral contraception before preg-					
nancy					
Yes	18 (5.1%)	34 (7.0%)	0.255	_	-
No	337 (94.9%)	453 (93.0%)		_	_

*Univariate analysis was used when the P value of Chi-square test was less than 0.05. The results were presented as OR with 95% CI.

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Table 4 Distribution of daily life	factors among hypertensive cases a	nd normotensive control su	bjects and crude estimation of
their associations			

	Chi-square test				
Factors	Case	Control	P value	Univariate analysis [*]	P value
	(<i>n</i> =373)	(<i>n</i> =507)			
Active smoking before pregnancy					
Yes	3 (0.8%)	9 (1.8%)	0.378	-	_
No	352 (99.2%)	489 (98.2%)		-	_
Active smoking in pregnancy					
Yes	0 (0.0%)	6 (1.2%)	0.097	-	_
No	360 (100%)	498 (98.8%)		_	-
Passive smoking before pregnancy					
Yes	201 (57.1%)	237 (48.2%)	0.010	1.43 (1.09, 1.89)	0.011
No	151 (42.9%)	255 (51.8%)		Reference	
Passive smoking in pregnancy					
Yes	201 (56.1%)	187 (37.4%)	< 0.001	2.14 (1.63, 2.83)	< 0.001
No	157 (43.9%)	313 (62.5%)		Reference	
Alcohol drinking in pregnancy					
Yes	9 (2.5%)	6 (1.2%)	0.158	-	_
No	357 (97.5%)	496 (98.8%)		_	_
Alcohol drinking before pregnancy					
Yes	47 (14.0%)	62 (13.8%)	0.939	-	_
No	288 (86.0%)	386 (86.2%)		_	_
Working in pregnancy					
Yes	259 (71.3%)	323 (65.0%)	0.049	_	_
No	104 (28.7%)	174 (35.0%)		-	_
Sleeping quality in pregnancy					
Poor	133 (36.9%)	266 (53.0%)	< 0.001	1.92 (1.46, 2.54)	< 0.001
Good	227 (63.1%)	236 (47.0%)		Reference	

*Univariate analysis was performed when the P value of Chi-square test was less than 0.05. The results were presented as OR with 95% CI.

Table 5 Disribution of psychosocial factors among hypertensive cases and normotensive control subjects and crud
estimation of their associations

	Chi-square test				
Factors	Case	Control	P value	Univariate analysis [*]	P value
	(<i>n</i> =373)	(<i>n</i> =507)			
Experience of anxiety					
Yes	113 (31.2%)	102 (20.4%)	< 0.001	1.77 (1.29, 2.41)	< 0.001
No	249 (68.8%)	249 (79.6%)		Reference	
Relationship with parents-in-law					
Poor	137 (38.1%)	81 (16.6%)	< 0.001	3.07 (2.24, 4.24)	< 0.001
Good	223 (61.9%)	406 (83.4%)		Reference	
Major stressful events in preg-					
nancy					
Yes	7 (1.9%)	4 (0.8%)	0.149	-	_
No	360 (98.1%)	497 (99.2%)		-	_
Severe dispute with husband in					
pregnancy					
Yes	18 (4.9%)	27 (5.4%)	0.078	-	_
No	349 (95.1%)	473 (94.6%)		_	_

^{*}Univariate analysis was used when the P value of Chi-square test was less than 0.05. The results were presented as OR with 95% CI.

Table 6 showed the statistical results for multivariable logistic regression analysis. All the factors with statistical significance were entered for multivariate logisitic regression analysis. The results showed that history of cardiovascular disease of her mother/brother/sister (OR=6.18, 95% CI, 2.37 to 16.14), history of pregnancy-induced hypertension (OR=16.64, 95% CI, 5.74 to 48.22), low maternal educational level (OR=2.81, 95% CI, 1.30 to 6.04), and poor relationship with their parents-in-law (OR=3.44, 95% CI, 1.55 to 7.59) were still statistically significant risk factors for hypertensive disorders in pregnancy. However, maternal age, pre-pregnancy body mass index, place of residence, paternal education level, family history of hypertension, passive smoking one year before and/or in pregnancy, and sleeping quality had no statistically significant associations with hypertensive disorders in pregnancy.

Variables	Mutlivariate analysis*	P value
History of cardiovascular diseases of her mother/brother/sister		
Yes	6.18 (2.37, 16.14)	< 0.001
No	Reference	
History of pregnancy-induced hypertension		
Yes	16.64 (5.74, 48.22)	< 0.001
No	Reference	
Maternal educational level		
Low	2.81 (1.30, 6.04)	0.008
High	Reference	
Relationship with parents-in-law		
Poor	3.44 (1.55, 7.59)	0.002
Good	Reference	

Table 6 Independent risk factors of hypertensive disorders among pregnant women

^{*}All the possible risk factors with P value less than 0.05 in univariate analysis were entered for multivariate analysis. The results were presented as OR with 95% CI.

3 DISCUSSION

The findings of our study demonstrated that history of cardiovascular diseases of her mother/brother/sister, history of previous pregnancy-induced hypertension, low maternal educational level and poor relationship with her parents-in-law were independent risk factors for hypertensive disorders in pregnancy.

History of previous pregnancy-induced hypertension was found to be the most powerful risk factor in our study (OR=16.64, 95% CI, 5.74 to 48.22). It suggested that the risk of recurrence of hypertensive disorders in pregnancy was substantial in subsequent pregnancies. Our result was in line with a large population-based multipurpose Tromsø Study, which suggested that gestational hypertension in first pregnancy increased the risk of recurrence in later pregnancy by 7.5-fold compared with a normotensive first pregnancy^[15].

Our findings regarding family history of cardiovascular disease suggested the involvement of genetic component in the multifactorial etiology of hypertensive disorders in pregnancy, which had also been indicated in previous researches^[12, 16–18]. However, most of the genetic involvement was concluded based on the family history of hypertension. Little investigation regarding the influence of family history of cardiovascular disease was available^[15, 19]. One population-based multipurpose Tromsø Study in 2012 revealed that women with gestational hypertension and preeclampsia more frequently reported a family history of stroke or brain hemorrhage angina pectoris, and myocardial infarction^[15]. It also revealed a secondary impact of hypertensive disorders in pregnancy on future cardiovascular diseases as other researches did^[15, 20, 21]. The awareness and implementation of follow-up care and counseling for hypertensive pregnant women may be needed to be infused into and carried out among obstetrician-gynecologists.

Besides, we found low maternal educational level to be significantly associated with hypertensive disorders in pregnancy among Chinese women. Other researches also found the negative impact of low maternal educational level on hypertensive disorders in pregnancy, in which one was a cohort study in Portugal population^[19] and another was a case-control study in Jordanian population^[23]. It is possible that mother with low educational level would lack awareness and behavior of perinatal care, resulting in delayed diagnosis, prevention and treatment of possible hypertensive disorders in pregnancy. In fact, insufficient perinatal care has been proved to be related to increased risk of developing hypertensive disorders in pregnancy^[22, 23].

Finally, we found that poor relationship with their parents-in-law had a statistically significant association

with hypertensive disorders in pregnancy. In China, it is a tradition that married women live together with their parents-in-law, especially during their pregnancies. Under this situation, poor relationship with their parents-in-law might lead to uncomfortable home environment and impose extra psychosocial burden on pregnant women. Evidence showed that psychosocial stress was associated with 1.6-fold increased risk for hypertensive disorders in pregnancy^[24]. Social support from women's partner^[25] and mindfulness-based intervention during pregnancy^[26] may be helpful to alleviate their psychosocial stress when such poor relationship occurs.

Furthermore, increased maternal age, increased pre-pregnancy body mass index, living in rural area, low paternal education level, family history of hypertension, passive smoking one year before and/or in pregnancy, and poor sleeping quality were found to be significantly associated with hypertensive disorder in pregnancy from univariate logistic analysis, while the association became uncertain when they were adjusted for confounders. In other researches, increased maternal age^[11, 27], increased pre-pregnancy body mass index^[28, 29], living in rural area^[23], family history of hypertension^[12, 17], and poor sleeping quality^[30] were found to be independent risk factors. The difference may be due to our small sample size. In future relevant researches, these risk factors should also be taken into consideration in case of small sample bias. With regard to passive smoking, despite robust literature has examined its influence on birth weight or prematurity^[31, 32], there are few studies on the influence of passive smoking on hypertensive disorders in pregnancy. Only one study involved this topic and revealed a relatively weak protective effect of passive smoking from hypertensive disorders^[33]. The role of passive smoking in hypertensive disorders needs to be elucidated in more rigorous researches in future. As for the influence of low paternal education, to our knowledge, there have been no studies on this aspect. It is possible that low paternal educational level would increase the risk of hypertensive disorders indirectly through their inability to give social support in stress situation for pregnant women. Maybe more researches are needed to confirm the effect of low paternal education on hypertensive disorders in pregnancy.

Our study has several limitations. Firstly, it was a case-control study, which may provide more optimistic results than cohort studies. Then, this study was performed in a limited geographic area so that the results may not be well generalized to other areas. Lastly, we mixed together the different types of hypertensive disorders, and the risk factors may not be specific to the sub-types of hypertensive disorders.

In summary, our study found that history of cardio-

vascular diseases of her mother/brother/sister, history of previous pregnancy-induced hypertension, low maternal educational level and poor relationship with her parents-in-law were independent risk factors for hypertensive disorders in pregnancy. Clinicians should pay attention to those risk factors in prenatal care for pregnant women in primary prevention. Besides, increased maternal age, increased pre-pregnancy body mass index, living in rural area, low paternal education level, family history of hypertension, and poor sleeping quality were possible risk factors while passive smoking was a possible protective factor. All of the potential risk factors were better to be taken into consideration in future researches and their influences on hypertensive disorders need to be elucidated.

Conflict of Interest Statement

The authors declare no conflict of interest.

REFERENCES

- National High Blood Pressure Education Group on High Blood Pressure in Pregnancy. Report of the National High Blood Pressure Education Program Working Group on High Blood Pressure in Pregnancy. Am J Obstet Gynecol, 2000,183(1):S1-S22
- 2 National Research Group on Hypertensive Disorders in Pregnancy. A nation-wide epidemiologic investigation of hypertensive disorders in pregnancy. Chin Obstet Gynecol (Chinese), 1991,26(2):67-71
- 3 Ma R, Liu JM, Li S, *et al.* Study on the descriptive epidemiology of pregnancy-induced hypertension from 1995–2000 in Jiaxing of Zhejiang province, China. Zhonghua Liu Xing Bing Xue Za Zhi (Chinese), 2005,26(12):960-963
- 4 Chang J, Elam-Evans LD, Berg CJ, *et al.* Pregnancy-related mortality surveillance--United States, 1991--1999. MMWR Surveil Summ, 2003,52(2):1-8
- 5 Khan KS, Wojdyla D, Say L, *et al.* WHO analysis of causes of maternal death: a systematic review. Lancet, 2006,367(9516):1066-1074
- 6 Qian D. Different levels of pregnancy-induced hypertension affect pregnancy outcomes observed. Chin Mod Doct (Chinese), 2013,51(36):157-159
- 7 He Y, Wen S, Tan H, *et al.* Study on the influence of pregnancy-induced hypertension on neonatal birth weight and its interaction with other factors. Zhonghua Liu Xing Bing Xue Za Zhi (Chinese), 2014,35(4):397-400
- 8 Macdonald-Wallis C, Tilling K, Fraser A, *et al.* Associations of blood pressure change in pregnancy with fetal growth and gestational age at delivery: findings from a prospective cohort. Hypertension, 2014,64(1):36-44
- 9 Ye C, Ruan Y, Zou L, *et al.* The 2011 survey on hypertensive disorders of pregnancy (HDP) in China: prevalence, risk factors, complications, pregnancy and perinatal outcomes. PloS One, 2014,9(6):e100180
- 10 Koelman CA, Coumans AB, Nijman HW, et al. Correlation between oral sex and a low incidence of preeclampsia: a role for soluble HLA in seminal fluid? J Reprod Immunol, 2000,46(2):155-166
- 11 Jasovic-Siveska E, Jasovic V, Stoilova S. Previous pregnancy history, parity, maternal age and risk of pregnancy induced hypertension. Bratisl Lek Listy, 2011,112(4):188-191
- 12 Zhao W, Wang JH. Screening program and risk factors on pregnancy-induced hypertension syndrome. Zhonghua Liu Xing Bing Xue Za Zhi (Chinese), 2004,25(10):845-847
- 13 Huang LY, Lu WL, Sun Z. Risk factors of pregnancy-induced hypertension syndrome: a meta analysis. Chin Prev Med J (Chinese), 2012,13(3):225-227

- 14 Cao Y. Chinese Obstetrics and Gynecology. Beijing: People's Medical Publishing House, 2007.
- 15 Andersgaard AB, Acharya G, Mathiesen EB, et al. Recurrence and long-term maternal health risks of hypertensive disorders of pregnancy: a population-based study. Am J Obstet Gynecol, 2012,206(2):143.e1-8
- 16 Mahomed K, Williams MA, Woelk GB, et al. Risk factors for preeclampsia-eclampsia among Zimbabwean women: recurrence risk and familial tendency towards hypertension. J Obstet Gynaecol, 1998,18(3):218-222
- 17 Poon LC, Kametas NA, Chelemen T, et al. Maternal risk factors for hypertensive disorders in pregnancy: a multivariate approach. J Hum Hypertens, 2010,24(2):104-110
- 18 Andelova K, Velebil P, Stroufova A, et al. Prediction of pregnancy-induced hypertension in women with risk factors. Ceska Gynekol, 1998,63(6):443-446
- 19 Alves E, Azevedo A, Rodrigues T, *et al.* Impact of risk factors on hypertensive disorders in pregnancy, in primiparae and multiparae. Ann Hum Biol, 2013,40(5): 377-384
- 20 Jonsdottir LS, Arngrimsson R, Geirsson RT, *et al.* Death rates from ischemic heart disease in women with a history of hypertension in pregnancy. Acta Obstet Gynecol Scand, 1995,74(10):772-776
- 21 Hermes W, Ket JC, van Pampus MG, *et al.* Biochemical cardiovascular risk factors after hypertensive pregnancy disorders: a systematic review and meta-analysis. Obstet Gynecol Surv, 2012,67(12):793-809
- 22 Suleiman AK. Risk factors on hypertensive disorders among Jordanian pregnant women. Glob J Health Sci, 2014,6(2):138-144
- 23 Luo B, Ma X. Risk factors for preeclampsia: a case-control study. Hypertens Pregnancy, 2013,32(4):432-438
- 24 Leeners B, Neumaier-Wagner P, Kuse S, *et al.* Emotional stress and the risk to develop hypertensive diseases in pregnancy. Hypertens Pregnancy, 2007,26(2):211-226
- 25 Cobb S. Social support as a moderator of life stress. Psychosom Med, 1976,38(5):300-314
- 26 Vieten C, Astin J. Effects of a mindfulness-based intervention during pregnancy on prenatal stress and mood: results of a pilot study. Arch Womens Ment Health, 2008,11(1):67-74
- 27 Chen CL, Cheng Y, Wang PH, et al. Review of pre-eclampsia in Taiwan: a multi-institutional study. Zhonghua Yi Xue Za Zhi (Chinese), 2000,63(12):869-875
- 28 Ehrenthal DB, Jurkovitz C, Hoffman M, *et al.* Pre-pregnancy body mass index as an independent risk factor for pregnancy-induced hypertension. J Womens Health, 2011,20(1):67-72
- 29 Li C, Zhang W. Effects of pre-pregnancy body mass index on pregnancy outcomes. Zhonghua Yi Xue Za Zhi (Chinese), 2014,94(1):36-38
- 30 Owusu JT, Anderson FJ, Coleman J, *et al.* Association of maternal sleep practices with pre-eclampsia, low birth weight, and stillbirth among Ghanaian women. Int J Gynaecol Obstet, 2013,121(3):261-265
- 31 Liu T, Chen W. Meta analysis of effects on maternal passive smoking during pregnancy on fetal low birth weight. J Hyg Res, 2009,38(6):677-681
- 32 Badlissi D, Guillemette A, Fadin A. Prematurity and low birth weight: effects of active and passive smoking during pregnancy. Can J Public Health, 2001,92(4):272-275
- 33 Engel SM, Scher E, Wallenstein S, *et al.* Maternal active and passive smoking and hypertensive disorders of pregnancy: risk with trimester-specific exposures. Epidemiology, 2013,24(3):379-380

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