Study on the influence of pregnancy-induced hypertension on neonatal birth weight

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ABSTRACT

To explore the effect of pregnancy-induced hypertension (PIH) on neonatal birth weight and provide the necessary reference value for the maternal and children health service. A cross-sectional study was carried out in Shaanxi Province of China in 2013. And a total of 28 045 singleton live infants and their mothers were recruited using a stratified, multistage, probability-proportional-to-size sampling method. Among the 28 045 women of childbearing age surveyed, multiple linear regression and quantile regression analysis all showed that the birth weight of newborns whose mothers had suffered from PIH during pregnancy was significantly lower than those whose mothers had not suffered from PIH during pregnancy from very low to higher birth weight percentiles (q=0–0.85), an average decrease of 137.45 g (β=−137.45, t=−5.77 and p<0.001). When birth weight was at q=0.90–1.00 percentiles, there was no birth weight difference between two groups. The present cross-sectional study indicated that PIH had an effect of on neonatal birth weight. When pregnant women with PIH are identified then the healthcare professional initiates a closer supervision of their pregnancy in order to ameliorate the status of BP and provide a good intrauterine environment for the fetus. In addition, the gynecologists should admonish the pregnant women that their health is related to the health of their fetus, then gravidas may be more engaged to alert their physician and accept early or preventative interventions. And the healthcare professional should ask and be alert to the issues of hypertension during pregnancy.

Significance of this study

What is already known about this subject?

- The present cross-sectional study indicated that pregnancy-induced hypertension (PIH) had an effect on neonatal birth weight.
- The birth weight of newborns whose mothers had suffered from PIH during pregnancy was significantly lower than those whose mothers had not suffered from PIH during pregnancy from very low to higher birth weight percentiles(q=0–0.85),
- Compared with the newborns whose mothers had not suffered from PIH, the birth weight of newborns whose mothers had suffered from PIH during pregnancy had an average decrease of 137.45 g (β=−137.45, t=−5.77 and p<0.001).

What are the new findings?

- Suffering from PIH during pregnancy can decrease the birth weight of newborns, and influence was greater in newborns with lower body weight than in newborns with higher body weight.
- The primary strength of the present analysis is the large sample size (28 045 single live births occurring from 2010 to 2013), which accounted for ~9% of neonates in Shaanxi Province. Therefore, our results can be generalized to the entire province as well as Northwest China.
- Traditional linear regression and quantile regression were used to study the association between the impact factors and birth weight of different percentiles in our study

INTRODUCTION

Birth weight is an important indication of mothers' and neonates' nutritional status and may be the important determinant of infant's survival, future health, growth, and development.[1] Low birth weight and large adult waist circumference increase the risk of neonatal death and cardiovascular disease.[2 3] According to the American College of Obstetricians and Gynecology (ACOG) practice bulletin, high birth weight easily lead to prolonged labor, postpartum hemorrhage, infection, perinatal asphyxia and so on.[4–6] Furthermore, macrosomic infants are at an increased risk of type 2 diabetes mellitus, hypertension, and obesity in adulthood.[7–12]

Hypertensive disorders complicating pregnancy, also known as pregnancy-induced hypertension (PIH) syndrome[13–15] is a complication of pregnancy which includes gestational hypertension, pre-eclampsia, eclampsia, pre-eclampsia complicated by chronic hypertension and chronic hypertension complicating pregnancy.[16 17] PIH complicates 3–5% of all

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Significance of this study

How might these results change the focus of research or clinical practice?

- The present cross-sectional study indicated that PIH had an effect on neonatal birth weight. The birth weights of newborns whose mothers had suffered from PIH during pregnancy were significantly lower than those whose mothers had not suffered from PIH from very low to higher percentiles(q=0~0.85). When pregnant women with PIH are identified then the healthcare professional initiates a closer supervision of their pregnancy in order to ameliorate the status of BP and provide a good intrauterine environment for the fetus. In addition, the gynecologists should admonish the pregnant women that their health is related to the health of their fetus, then gravidas may be more engaged to alert their physician and accept early or preventative interventions. And the healthcare professional should ask and be alert to the issues of hypertension during pregnancy. Hence, this is a timely topic; the relationship between hypertension and an optimal intrauterine environment requires further exploration.

pregnancies and is a major cause of perinatal morbidity and mortality.[18 19]

The human placenta is a dynamic and heterogeneous organ critical in the establishment of the fetomaternal interface and the maintenance of gestational well-being.[20] Placental dysfunction contributes to significant complications, such as pre-eclampsia, a potentially lethal hypertensive disorder during pregnancy. Previous studies have identified significant changes in the expression profiles of pre-eclamptic placentas using whole-tissue analysis.[21 22] In addition, placental dysfunction affects the fetus, causing prematurity[23] and fetal growth and neurodevelopmental abnormalities.[24] Kabir's study concluded that increment of birth weight occurs with increase in placental weight. And, if placental weight can be measured by ultrasonography in second or early third trimester of pregnancy, birth weight is possible to be assessed and appropriate measure can be taken to increase the birth weight.[25] So hypertensive disorders in pregnancy are related to placenta and therefore are related indirectly to the nutrition and weight of the fetus.

PIH is a well-recognized predictor of infant birth weight. The effects of PIH on birth weight have also been shown in prior analyses. Phad's study indicated that PIH influenced the growth and development of both the placenta and fetus. And compared with normotensive pregnancies, the result showed that the median weight of the placenta and neonatal birth weight were all significantly lower in the PIH group.[26] Moreover, the researches demonstrated that the risk of low birthweight infants born to mothers among pregnant women with PIH is higher than that of pregnant women without PIH.[27 28]

Despite extensive research on the influence of PIH on neonatal birth weight, there has not been a large sample cross-sectional investigation to analyse the association between PIH and neonatal birth weight. Therefore, a large population-based sampling survey which was conducted in Shaanxi Province to assess birth outcomes allowed us to study the influence of PIH on neonatal birth weight.

MATERIALS AND METHODS

Study design and participants

The present cross-sectional study was carried out in Shaanxi Province of Northwest China from August to November 2013. The infants and young children born during 2010–2013 and their mothers were randomly sampled. Considering the population density and fertility rates (~9.73%)[29] of the rural and urban areas in the whole province, a stratified multistage, probability-proportional-to-size sampling method was adopted in the present study. In China, the administrative structure was divided into three-level frames. The rural areas consisted of counties, townships and villages. Independent of rural areas, the urban areas consisted of districts, streets and communities. As a first step, we randomly selected 20 counties and 10 districts from the whole province. In the next step, six townships and three streets from the chosen counties and districts were randomly sampled, respectively. Then we randomly selected six villages from each chosen township and six communities from each chosen street. A random sampling method was adopted to severally select 30 babies in each sampled village and 60 babies in each chosen community who were born between 2010 and 2013, and their mothers were also chosen. We expected approximately 32 400 infants and their mothers to be absorbed in our project. However, 2373 objects of the randomly selected population refused to participate (response rate: 92.68%). Hence, 28 644 single live infants were considered for this study. And 599 subjects were removed for unknown birth weight and PIH. Eventually, a total of 28 045 single live infants were selected.

Data collection

All data including sociodemographical characteristics and maternal lifestyles during pregnancy was stated by the mothers of the selected children. Xi'an Jiaotong University Health Science Center designed all questionnaires. Ten field teams consisted of 10–12 trained investigators. As soon as every questionnaire was completed, the supervisors were responsible for checking any mistakes and/or imperfect information. All data collection was completed in the local village clinics and community health service centers. Our work received the support of the local hospitals and health administrative departments as well as the Shaanxi Province Ministry of Health. Written informed consent was obtained from all study participants after a detailed briefing on the purpose, process and confidentiality of the research.

Cohort criteria

- Women of childbearing age (15–49 years) and their children who were born in 2010–2013.
- Residents in research area.

PIH diagnostic criteria

According to Obstetrics and Gynecology (the eighth edition),[16] hypertensive disorder complicating pregnancy is a group of diseases coexisting with pregnancy and hypertension. The basic pathophysiological changes of the

Table 1 Characteristics of the study population

Baseline characteristics	No-PIH	PIH	t/χ^2	P values
Maternal age, year*	27.04 (4.72)	28.59 (5.57)	−5.35	<0.001
Gestational age, week*	39.66 (1.24)	38.90 (2.06)	7.18	<0.001
Sex of infants, n (%)				
Boy	15 060 (54.44)	204 (53.54)	0.12	0.727
Girl	12 604 (45.56)	177 (46.46)		
Season of birth, n (%)				
Spring	7095 (25.65)	120 (31.50)	10.33	0.016
Summer	6645 (24.02)	73 (19.16)		
Fall	6865 (24.82)	84 (22.05)		
Winter	7059 (25.51)	104 (27.29)		
Region, n (%)				
Central Shaanxi	14 986 (54.17)	222 (58.27)	8.95	0.011
Northern Shaanxi	7073 (25.57)	72 (18.90)		
Southern Shaanxi	5605 (20.26)	87 (22.83)		
Mother's education, n (%)				
Primary school or less	3269 (11.84)	48 (12.60)	2.77	0.429
Junior high school	13 692 (49.61)	182 (47.77)		
Senior high school	5573 (20.19)	70 (18.37)		
College and above	5068 (18.36)	81 (21.26)		
Residence, n (%)				
Urban area	5706 (20.71)	91 (23.88)	2.30	0.129
Rural area	21 846 (79.29)	290 (76.12)		
Mother's occupation, n (%)				
Peasant/housework	9858 (35.88)	136 (35.70)	0.01	0.941
Other	17 618 (64.12)	245 (64.30)		
Household Wealth Index, n (%)				
Poorest	6367 (25.24)	78 (21.97)	2.01	0.367
Middle income	13 561 (53.75)	198 (55.77)		
Richest	5301 (21.01)	79 (22.26)		
Parity				
1	16 395 (59.26)	213 (55.91)	1.76	0.185
≥2	11 269 (40.74)	168 (44.09)		

*Reported as mean and SD.
PIH, pregnancy-induced hypertension.

disease are small vessel spasm, endothelial injury and focal ischemia. Also, the main clinical manifestations are hypertension, proteinuria and severe convulsions. PIH includes gestational hypertension, pre-eclampsia, eclampsia, pre-eclampsia complicated by chronic hypertension and chronic hypertension complicating pregnancy.

Statistical analysis

A database was designed using EpiData V.3.02, and data entry was duplicated. Initially, the characteristics of participants were described using means±SD for normally distributed continuous variable. The categorical variables were analysed using counts and proportions. The percentage differences between groups were proved using the χ^2 test. The birth weight of newborns and PIH during pregnancy were used as the dependent variables and independent variables, respectively, in multiple linear regression model and quantile regression model, and confounding factors were controlled. Using the PROC QUANTREG process in SAS V.9.4 software, the internal point method was used to fit the quantile regression model of birth weight at different percentile (q=0.05, 0.10, 0.15, 0.20, 0.25, 0.30, 0.35, 0.40, 0.45, 0.50, 0.55, 0.60, 0.65, 0.70, 0.75, 0.80, 0.85, 0.90, 0.95). All statistical analyses were performed using SAS V.9.4. Two-tailed $p<0.05$ was considered statistically significant.

RESULT

Baseline characteristics of the participants

Among the 28 045 women of childbearing age surveyed, 381 (1.36%) women with PIH were included. Of the infants, boys accounted for 54.43% of total infants. Among the region of the infants, infants in Central Shaanxi, Northern Shaanxi and Southern Shaanxi accounted for 54.23%, 25.48% and 20.29%, respectively. The childbearing age of mothers was 27.06±4.74 years and approximately 38.57% of them were educated beyond senior high school. The other details of the sample and distribution of the major demographic variables are shown in table 1.

Status of neonatal birth weight

The average birth weight of 28 045 newborns was 3267.80±456.43 g. The neonatal average birth weight of

Table 2 The influence of pregnancy-induced hypertension (PIH) on birth weight

Pregnant women	N	Normal	Low birth weight	Macrosomia
No-PIH	27 664	24 864 (89.88)	898 (3.25)	1902 (6.87)
PIH	381	316 (82.94)	43 (11.29)	22 (5.77)
Total	28 045	25 180 (89.78)	941 (3.36)	1924 (6.86)
χ^2	75.08			
P value	<0.001			

the women with PIH was 3097.22±573.90 g and that of the women with no-PIH was 3270.15±454.17 g. Neonatal average birth weight of women with no-PIH was higher than that of women with PIH, and the difference was statistically significant. The birth weight status of the children for two groups were shown in table 2. The distribution of birth weight in PIH group is different from that in no-PIH group, and the difference was statistically significant ($p<0.001$).

Univariate analysis of influencing factors of neonatal birth weight

Univariate analysis results showed that there were statistically significant effects of maternal age ≥35 years, peasant/housework, living in rural areas, PIH and a total of 14 factors on neonatal birth weight (table 3).

Multivariate analysis of the effect of PIH on neonatal birth weight

The birth weight of newborns and PIH during pregnancy were used as the dependent variables and independent variables, respectively, in multiple linear regression model and quantile regression model, and confounding factors were controlled. Multiple linear regression analysis showed that the birth weight of newborns whose mothers had suffered from PIH during pregnancy were significantly lower than those whose mothers had not suffered from PIH during pregnancy, an average decrease of 137.45 g ($\beta=-137.45$, $t=-5.77$ and $p<0.001$). Quantile regression analysis showed that the birth weights of newborns whose mothers

Table 3 Univariate analysis of possible influencing factors on birth weight

Variables	Group	Birth weight, g (mean±SD)	t/F	P values
Maternal age	<35	3270.61±452.73	3.43	0.001
	≥35	3232.30±495.24		
Gestational week	<37 weeks	2725.84±651.98	598.42	<0.001
	≥37 weeks and <42 weeks	3279.85±439.86		
	≥42 weeks	3400.54±442.15		
Sex	Boy	3321.64±456.00	21.80	<0.001
	Girl	3203.49±448.57		
Season of birth	Spring	3275.46±455.52	4.18	0.006
	Summer	3272.91±448.72		
	Fall	3271.70±455.02		
	Winter	3251.49±465.50		
Mother's education	Primary school or less	3198.20±488.79	73.62	<0.001
	Junior high school	3251.05±449.96		
	Senior high school	3288.74±445.09		
	College and above	3334.98±455.43		
Residence	Urban area	3336.71±463.99	12.79	<0.001
	Rural area	3249.58±452.87		
Mother's occupation	Peasant/Housework	3248.29±456.55	9.45	<0.001
	Other	3302.10±454.64		
Wealth Index	Poorest	3232.20±458.50	54.52	<0.001
	Middle	3262.18±455.08		
	Richest	3318.92±452.95		
Parity	1	3262.63±452.38	−2.28	0.023
	≥2	3275.30±462.17		
Maternal passive smoking	No	3274.49±453.81	4.41	<0.001
	Yes	3243.04±465.82		
Pregnancy-induced hypertension	No	3270.15±454.17	5.86	<0.001
	Yes	3097.22±573.90		
Taking nutrients	No	3227.72±477.32	−5.71	<0.001
	Yes	3274.52±452.16		
Pesticide	No	3269.21±456.05	4.81	<0.001
	Yes	3137.89±475.02		
Drug	No	3270.50±454.23	2.30	0.021
	Yes	3253.12±467.68		

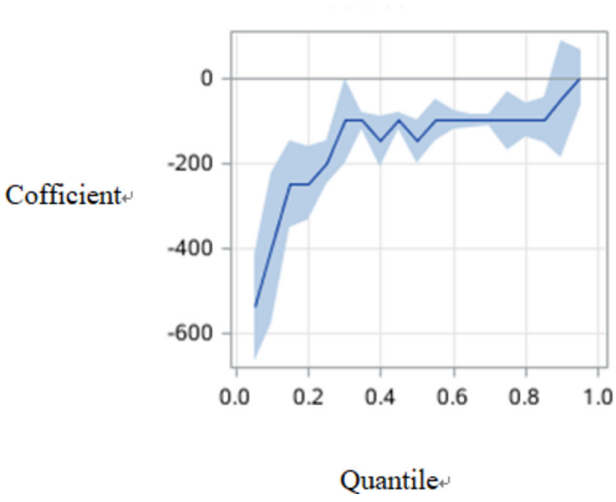

Figure 1 The effect of pregnancy-induced hypertension (PIH) on birth weight in different percentile. The shaded part was the 95% CI of the regression coefficient, and the reference group was no-PIH group which had not suffered from PIH during pregnancy.

had suffered from PIH during pregnancy were lower than those whose mothers had not suffered from PIH from very low to higher percentiles(q=0–0.85), the difference was significant. When birth weight was at q=0.90–1.00 percentiles, there was no birth weight difference between two groups. Suffering from PIH during pregnancy can decrease the birth weight of newborns, and influence was greater in newborns with lower body weight than in newborns with higher body weight (figure 1, table 4).

Table 4 Relationship between pregnancy-induced hypertension and birth weight in different percentiles

Quantile	β (95% CI)	$S_{\bar{X}}$	t	P values
0.05	−540.00 (−667.31 to −412.69)	64.95	−8.31	<0.001
0.10	−400.00 (−577.56 to −222.44)	90.59	−4.42	<0.001
0.15	−250.00 (−350.83 to −149.17)	51.44	−4.86	<0.001
0.20	−250.00 (−336.42 to −163.58)	44.09	−5.67	<0.001
0.25	−200.00 (−251.14 to −148.86)	26.09	−7.67	<0.001
0.30	−100.00 (−200.06 to −10.06)	51.05	−2.56	0.010
0.35	−100.00 (−119.80 to −80.20)	10.10	−9.90	<0.001
0.40	−150.00 (−211.41 to −88.59)	31.33	−4.79	<0.001
0.45	−100.00 (−119.80 to −80.20)	10.10	−9.90	<0.001
0.50	−150.00 (−202.61 to −97.39)	26.84	−5.59	<0.001
0.55	−100.00 (−149.56 to −50.44)	25.29	−3.95	<0.001
0.60	−100.00 (−123.40 to −76.60)	11.94	−8.38	<0.001
0.65	−100.00 (−115.66 to −84.34)	7.99	−12.51	<0.001
0.70	−100.00 (−114.03 to −85.97)	7.16	−13.97	<0.001
0.75	−100.00 (−168.95 to −31.05)	35.18	−2.84	0.005
0.80	−100.00 (−138.26 to −61.74)	19.52	−5.12	<0.001
0.85	−100.00 (−153.24 to −46.76)	27.16	−3.68	<0.001
0.90	−50.00 (−187.44 to 87.44)	70.12	−0.71	0.476
0.95	0.00 (−64.82 to 64.82)	33.07	0.00	1.000

Multiple linear regression and quantile regression analysis adjusted for season of birth, gestational age, sex of infants, parity, taking nutrients during pregnancy, mother's relevant characteristics (including mother's age, education level and occupation), maternal exposure history of risk factors (including pesticides, passive smoking, taking medications) and status of family characteristics (including economic conditions and residence).

DISCUSSION

Main findings

Birth weight is an important index to measure the intrauterine growth of the fetus, and it is also an indicator of the economic status of a country. We found that the birth weight of newborns whose mothers had suffered from PIH during pregnancy were significantly lower than those whose mothers had not suffered from PIH during pregnancy, an average decrease of 137.45 g (β=−137.45, t=−5.77 and p<0.001). Suffering from PIH during pregnancy can decrease the birth weight of newborns, and influence was greater in newborns with lower body weight than in newborns with higher body weight.

When pregnant women with PIH are identified then the healthcare professional initiates a closer supervision of their pregnancy in order to ameliorate the status of BP and provide a good intrauterine environment for the fetus. Maybe it is important for healthcare professional to monitor BP of the pregnant women and provide adequate prenatal care for them. In addition, the gynecologists should admonish the pregnant women that their health is related to the health of their fetus, then gravidas may be more engaged to alert their physician and accept early or preventative interventions. And the healthcare professional should ask and be alert to the issues of hypertension during pregnancy. Hence, this is a timely topic; the relationship between hypertension and an optimal intrauterine environment requires further exploration.

Data interpretation and comparisons with previous studies

The effect of PIH on neonatal birth weight has been previously investigated in a few studies conducted elsewhere. Some previous studies have also proved that hypertensive disorders in pregnancy are related to placenta, and placenta is associated with the nutrition and weight of the fetus.[22 24 25] Therefore, PIH are related indirectly to the nutrition and weight of the fetus. A study reported by Xiong *et al*[30] identified that gestational hypertension was associated with a slightly increased risk of intrauterine growth restriction (adjusted OR 1.49 (95% CI 1.14 to 1.93)). He's study illuminated that PIH was associated with the incidence of low birth weight infants and macrosomias.[31] Moreover, PIH was also believed to be associated with an increased risk of poor fetal growth.[32 33] The aforementioned studies illuminated the relationship between PIH and neonatal birth weight and provided some references and evidence for our research.

Strengths and limitations

The primary strength of the present analysis is the large sample size (28 045 single live births occurring from 2010 to 2013), which accounted for ∼9% of neonates in Shaanxi Province.[29] Therefore, our results can be generalized to the entire province as well as Northwest China. Another strength of this study is that the birth weight data collected from birth certificates was precise to the nearest 10 g. Moreover, for the analysis of birth weight, traditional linear regression can only examine the relationship between the impact factors and the birth weight. However, both traditional linear regression and quantile regression were used to study the association between the impact factors and birth weight of different percentiles in our study. And it

steadily displayed that low birth weight and macrosomia, both ends of the birth weight, which were focused by us, were affected by independent variables. The two regression were used to avoid the traditional linear regression based on ordinary least squares underestimating or overestimating the effects of independent variables on low weight and very high weight. Limitations of our data should also be noted. Some major confounders, including pre-pregnancy BMI, diet, weight gain during pregnancy[34 35] and so on, were not adjusted for because we lacked these data. Besides, we conducted face-to-face interview based on a cross-sectional survey of a larger sample, and manpower, material and financial resources were not enough to support us to ask disease history in detail or browse the medical records at that time. It is unavoidable that the recall bias existed, because women or her family members answered the questions by recalling. So some women with PIH were missed and which lead to a very small incidence rate of PIH. Nevertheless, the current study is the first and largest survey that has presently been conducted in Northwest China and provides the best information on the influence of PIH on neonatal birth weight in this geographical region.

CONCLUSIONS

The present cross-sectional study indicated that PIH had an effect on neonatal birth weight. The birth weights of newborns whose mothers had suffered from PIH during pregnancy were significantly lower than those whose mothers had not suffered from PIH from very low to higher percentiles (q=0–0.85). When pregnant women with PIH are identified then the healthcare professional initiates a closer supervision of their pregnancy in order to ameliorate the status of BP and provide a good intrauterine environment for the fetus. In addition, the gynecologists should admonish the pregnant women that their health is related to the health of their fetus, then gravidas may be more engaged to alert their physician and accept early or preventative interventions. And the healthcare professional should ask and be alert to the issues of hypertension during pregnancy. Hence, this is a timely topic; the relationship between hypertension and an optimal intrauterine environment requires further exploration.

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Competing interests None declared.

Patient consent Parental/guardian consent obtained.

Ethics approval The survey was approved by the Ethic Review Committee and Academic Committee, Xi'an Jiaotong University College of Medicine, Xi'an, China.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement The data collection has been acomplished together by the research team, and the research team has contributed a lot of effort for it. Therefore, this data was kept by the project group, and corresponding authors could been contacted for data information where needed.

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