MEDICAL SCIENCE MONITOR

CLINICAL RESEARCH

e-ISSN 1643-3750
© Med Sci Monit, 2020; 26: e927409
DOI: 10.12659/MSM.927409

Received: 2020.07.13
Accepted: 2020.09.08
Available online: 2020.09.17
Published: 2020.11.09

Weight Gain Before the Third Trimester and Risk of Hypertensive Disorders of Pregnancy: A Prospective Cohort Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1,2 Xiaoyi Zou
ACDG 3 Ning Yang
B 4 Wei Cai
B 5 Xiulong Niu
CD 6 Maoti Wei
B 4 Xin Zhang
CD 7 Xuejing Hou
B 8 Fang Kang
AG 9 Yuming Li

1 Graduate School, Tianjin Medical University, Tianjin, R.P. China
2 Tianjin Key Laboratory of Cardiovascular Remodeling and Target Organ Injury, Characteristic Medical Center of PAP, Tianjin, R.P. China
3 Department of Hypertension, Tianjin Economic-Technological Development Area (TEDA) International Cardiovascular Hospital, Tianjin, R.P. China
4 Department of Prevention and Therapy of Cardiovascular Diseases in Alpine Environment of Plateau, Characteristic Medical Center of PAP, Tianjin, R.P. China
5 Department of Prevention and Therapy of Skin Disease in the Security Environment, Characteristic Medical Center of PAP, Tianjin, R.P. China
6 Center of Clinical Epidemiology, Tianjin Economic-Technological Development Area (TEDA) International Cardiovascular Hospital, Tianjin, R.P. China
7 Department of Obstetrics, The First Hospital of Qinhuangdao, Hebei province, R.P. China
8 Cardiovascular Disease Integrated Department, Tianjin Economic-Technological Development Area (TEDA) International Cardiovascular Hospital, Tianjin, R.P. China
9 Department of Cardiology, Tianjin Economic-Technological Development Area (TEDA) International Cardiovascular Hospital, Tianjin, R.P. China

Corresponding Author: Yu-ming Li, e-mail: cardiolab@163.com

Source of support: The study was supported by Tianjin Municipal Science and Technology Committee (grant no. 15ZXJZSY00010), Tianjin Science and Technology Project (grant no. 16ZXMJSY00 130), and National Key Research and Development Program of China (grants no. 2017YF C1307600 and 2017YFC1307602)

Background: The association between excessive gestational weight gain (GWG) and the risk of hypertensive disorders of pregnancy (HDP) remains uncertain in women with increased water retention in late gestation associated with the pathophysiology of HDP. This study aimed to investigate the association between GWG before the third trimester and the risk of HDP.

Material/Methods: This was a prospective cohort study in singleton-pregnant women in Tianjin, China, from 2016. Generalized linear models were used to analyze the relationship between weight gain and the risk of HDP.

Results: A total of 5295 singleton-pregnant women were included. Even after adjusting for relevant confounders, weight gain at approximately 28 weeks remained an independent risk factor for HDP in the normal-weight group. Compared to the reference of low weight gain (<–1 SD), weight gain >+1 SD was associated with an approximately 2.0 times greater likelihood of HDP (RR: 2.08, 95% CI: 1.06–4.08). Moreover, there was a positive relationship between weight gain in the short interval of early pregnancy and risk of HDP in overweight women.

Conclusions: Excessive weight gain before the third trimester was associated with a greater risk of developing HDP among women with early-pregnancy normal weight, which may provide a chance to identify subsequent hypertensive disorders. Additional research is needed to determine whether early-pregnancy weight gain is associated with HDP risk.

MeSH Keywords: **Body Mass Index • Hypertension, Pregnancy-Induced • Obesity • Pre-Eclampsia • Weight Gain**

Abbreviations: **HDP** – hypertensive disorders of pregnancy; **BMI** – body mass index; **GWG** – gestational weight gain; **SD** – standard deviation; **RR** – relative risk; **CI** – confidence interval; **IOM** – Institutes of Medicine

Full-text PDF: https://www.medscimonit.com/abstract/index/idArt/927409

3208 4 1 22

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Background

Hypertensive disorders of pregnancy (HDP), including gestational hypertension, preeclampsia, and eclampsia, are high-risk factors for future cardiovascular events in women [1,2]. Studies have shown that women with HDP and their offspring have significantly higher risks of cardiovascular events in the future [3–5]; therefore, early diagnosis and prevention of HDP may improve their long-term health. Obesity has been reported to be a modifiable risk factor for HDP in several studies [6–8], but the association between excessive gestational weight gain and the risk of HDP remains uncertain or insufficient [9–11]; greater weight gain is related to a longer pregnancy duration and edema during pregnancy, mainly in the third trimester. Considering HDP as a disorder typically identified by new-onset hypertension in the second half of pregnancy, mainly in the third trimester, the relationship between weight gain before the third trimester and the incidence of HDP are uncertain, and there have been few studies on this topic in the Chinese population.

Conventional measures of gestational weight gain (GWG) can introduce bias into epidemiologic studies of GWG and adverse perinatal outcomes, such as premature birth, neonatal death, stillbirth, and preeclampsia, because both are correlated with gestational duration [10,12,13]. The gestational age-specific z-score of weight gain is a new measure to evaluate weight gain, which is independent of gestational duration. Compared with GWG, it correlates better with preterm birth [12]. Whether the gestational age-specific z-score of weight gain is suitable to assess the risk of HDP remains undetermined.

The main aim of the present study was to assess weight gain in 4 gestational periods 16 weeks (14^{+0}, 17^{+6}), 20 weeks (18^{+0}, 21^{+6}), 24 weeks (22^{+0}, 25^{+6}), and 28 weeks (26^{+0}, 29^{+6}) – and the risk of HDP in 4 early-pregnancy BMI categories – 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)]. We also aimed to assess these relationships using the gestational age-specific z-score for weight gain.

Material and Methods

Study design

This was a prospective cohort study of singleton-pregnant women in Tianjin, China, from 2016. This study was approved by the Medical Ethics and Human Clinical Trial Committee of the local hospital, and all participants agreed to participate in the study and signed a written informed consent form. Participants were recruited from 19 community hospitals if they met the following criteria:

Inclusion criteria: (I) Singleton pregnancy; (II) Gestational age at enrolment <13 completed weeks; and (III) No presence of chronic hypertension. Exclusion criteria: (I) Incomplete or abnormal enrolment information or follow-up information; (II) Pregnancy termination for various reasons before 24 weeks of pregnancy; and (III) Systolic blood pressure ≥140 mmHg (1 mmHg=0.133 kPa) and/or diastolic blood pressure ≥90 mmHg before 20 weeks of pregnancy.

The participants completed a pre-designed questionnaire to collect baseline characteristics, including age, ethnicity, education level, family history, pregnancy, and delivery times. Height and weight at enrolment were simultaneously recorded. Gestational age was calculated according to the last menstrual period and checked by B-ultrasonic examination in early pregnancy. Pregnant women were followed up once every 4 weeks up to 28~30 weeks of gestation, and the diagnoses were recorded by the medical record system of the hospitals for delivery.

Observation outcomes

The early pregnancy BMI was calculated based on maternal height and weight recorded at the first prenatal visit. Gestational weight gain was defined as the difference between the weight at the corresponding gestational age and the weight at the first prenatal visit. Patients with weight gain above or below 4 SD of each group at each gestational age were flagged and excluded according to their weight trajectory and clinical plausibility. If there were multiple weight measurements during some periods, the last one was analysed. The weight gain z-score was calculated using BMI-specific z-score charts for Chinese women [14]. The z-scores were analysed as continuous variables and categorical variables, referring to the method used by Bodnar et al. [11]; the weight gain z-score was modelled as a 3-level categorical variable (<–1 SD, –1 to +1 SD, >+1 SD), where <–1 SD was the reference category, which was assumed to indicate low HDP risk.

The diagnostic criteria for HDP were based on the Guidelines for the Diagnosis and Treatment of Hypertensive Disorders in Pregnancy (2015) [15]. Gestational hypertension was defined as a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg after 20 weeks of pregnancy, which returned to normal within 12 weeks after delivery, and a negative urine protein test. Preeclampsia was defined as a systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg after 20 weeks of pregnancy accompanied by any of the following: urine protein ≥0.3 g/24 h, urine protein/creatinine ratio ≥0.3, random urine protein ≥(+) (examination method when urinary protein quantification could not be performed), or no proteinuria but heart, lung, liver, kidney or other important organ involvement or abnormal changes in the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

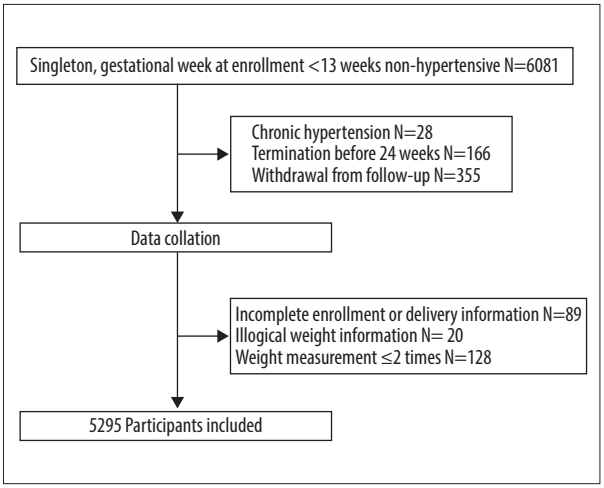

Figure 1. Study flowchart.

blood system, digestive system, nervous system, or the fetus. Eclampsia was defined as seizures that occurred during preeclampsia that could not be explained by other causes.

Statistical analyses

Quartiles and percentage counts were used to describe the baseline characteristics of pregnant women. Non-parametric tests and chi-square tests were used to analyze the differences between groups. Relative risks (RRs) with 95% confidence intervals (CIs) were obtained using general linear models to analyse the relationship between weight gain or weight gain z-scores at the corresponding gestational week and the risk of HDP. Moreover, analyses were adjusted for the age at enrolment, early-pregnancy BMI, primipara, and family history of hypertension. Statistical analyses were performed using SPSS version 23.0 (IBM Corp, Armonk, NY, USA) and STATA version 14.0 (Stata Corp, College Station, TX, USA).

Results

A total of 6081 non-hypertensive singleton-pregnant women with a gestational age at enrolment of <13 completed weeks were enrolled. Among these women, 28 were eventually diagnosed with chronic hypertension or chronic hypertension complicated with preeclampsia; 166 women had terminated pregnancies for various reasons before 24 weeks; 355 women withdrew from follow-up or were lost to follow-up; 109 participants had incomplete enrolment or delivery information or illogical weight records; and 128 participants had ≤2 weight measurements in the 4 periods. Finally, 5295 pregnant women were included. The study flowchart is outlined in Figure 1.

The characteristics of the 5295 women who participated in the study are presented in Table 1. Among them, 512 (9.7%), 3231 (61.0%), 1156 (21.8%), and 396 (7.5%) women were underweight, normal-weight, overweight, and obese, respectively. There were 177 cases of preeclampsia, 3 cases of eclampsia, and 105 cases of gestational hypertension. The total incidence of HDP was 5.4%. The corresponding incidence rates of HDP in the underweight, normal-weight, overweight, and obese groups were 2.3%, 3.5%, 9.3%, and 13.1%, respectively. In this Chinese cohort, 96% were of Han ethnicity, which is the ethnic majority in China, and 69% were nulliparous. The mean maternal age at enrolment was 30 years. With the increase in early-pregnancy BMI, the chance of developing HDP gradually increased, and the mean weight gain during each gestational period gradually decreased. However, there was no significant difference in weight gain z-scores between the 4 BMI groups.

Tables 2 and 3 compare the characteristics of women with or without HDP overall and in each BMI group. Overall, compared to women who did not progress to HDP, women who eventually progressed to HDP had higher early-pregnancy BMIs, were more likely to be primipara, and had family histories of hypertension and caesarean section, but they had a lower gestational age at delivery and lower neonatal weight. There were no statistically significant differences in education level, gestational age at enrolment, or neonatal sex. In the underweight group, only weight gain and weight gain z-scores of women with HDP at approximately 28 weeks were higher than those of the control group, and there were no significant differences in the other parameters. In the normal-weight group, which accounted for 61% of the entire cohort, weight gain in women with HDP at approximately 24–28 weeks and weight gain z-scores at approximately 28 weeks were higher than those of the control group. In the overweight and obese groups, weight gain and weight gain z-scores of women with HDP at approximately 16 weeks were higher than those of normotensive women in the overweight group, while the opposite result was obtained in the obese group. There were no significant differences in weight gain and the weight gain z-scores in the other periods.

Crude and adjusted RRs for weight gain or weight gain z-scores before the third trimester and the risk of HDP according to early-pregnancy BMI category are shown in Table 4. In underweight women, weight gain at approximately 28 weeks was positively correlated with the risk of HDP (crude RR: 1.23, 95% CI: 1.02–1.47). After adjusting for confounding factors, such as age, early pregnancy BMI, primipara, and family history of hypertension, the adjusted RR was 1.21 (95% CI: 1.01–1.45). The association of the weight gain z-score at approximately 28 weeks with the risk of HDP was null. Considering the small sample and the low incidence of HDP in the underweight group, the test efficiency may have been insufficient. Weight gain and weight gain z-scores at approximately 28 weeks in the normal-weight group were associated with the risk of HDP

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 1. Baseline characteristics of pregnancies according to early-pregnancy BMI category.

Characteristics	Total	Under Weight	Normal Weight	Overweight	Obese	P
Sample	n=5295	n=512	n=3231	n=1156	n=396	
HDP	285 (5.4%)	12 (2.3%)	113 (3.5%)	108 (9.3%)	52 (13.1%)	0.000
Age (year)	30 (28, 33)	29 (27, 31)	30 (28, 33)	31.0 (29, 34)	31 (29, 34)	0.000
Ethnicity (Han)	5084 (96.0%)	494 (96.5%)	3093 (95.7%)	1112 (96.2%)	385 (97.2%)	0.459
Education level (year)						0.000
≤9	909 (17.2%)	87 (17.0%)	490 (15.2%)	224 (19.4%)	108 (27.3%)	
9 to 12	3809 (71.9%)	375 (73.2%)	2354 (72.9%)	816 (70.6%)	264 (66.7%)	
>12	577 (10.9%)	50 (9.8%)	387 (12.0%)	116 (10.0%)	24 (6.1%)	
Primipara	3656 (69.0%)	414 (80.9%)	2247 (69.5%)	739 (63.9%)	256 (64.6%)	0.000
Family history of hypertension	995 (18.8%)	82 (16.0%)	571 (17.7%)	248 (22.5)	94 (23.7%)	0.001
BMI at enrolment, kg/m^2	21.9 (19.9, 24.5)	17.7 (17.1, 18.2)	21.1 (19.9, 22.4)	25.4 (24.7, 26.6)	29.9 (28.7, 31.3)	0.000
GW at enrolment, week	11^{+0} (9^{+5}, 12^{+1})	11^{+1} (10^{+0}, 12^{+2})	11^{+0} (9^{+5}, 12^{+1})	10^{+6} (9^{+5}, 12^{+1})	11^{+2} (9^{+5}, 12^{+1})	0.289
GW at delivery, week	39^{+2} (38^{+4}, 40^{+1})	39^{+3} (38^{+5}, 40^{+2})	39^{+3} (38^{+4}, 40^{+2})	39^{+2} (38^{+3}, 40^{+1})	39^{+0} (38^{+2}, 39^{+6})	0.000
Caesarean section	2720 (51.4%)	178 (34.8%)	1542 (47.7%)	705 (61.0%)	295 (74.5%)	0.000
Neonatal sex (Male)	2807 (53.0%)	264 (51.6%)	1682 (52.1%)	629 (54.4%)	232 (58.6%)	0.059
Neonatal height, cm	50 (50, 51)	50 (49, 50)	50 (50.51)	50 (50, 51)	50 (50, 51)	0.000
Neonatal weight, g	3360 (3070, 3650)	3215 (2980, 3450)	3340 (3055, 3600)	3440 (3150, 3730)	3495 (3180, 3820)	0.000
Neonatal score	10 (9, 10)	10 (9, 10)	10 (9, 10)	10 (9, 10)	10 (9, 10)	0.279
GWG						
16 weeks, kg	1.0 (0.3, 2.0)	1.5 (0.5, 2.5)	1.0 (0.5, 2.0)	1.0 (0.2.0)	1.0 (0.2.1)	0.000
20 weeks, kg	3.5 (2.3, 5.0)	4.0 (3.0, 5.5)	3.8 (2.5, 5.0)	3.3 (2.0, 4.8)	2.5 (1.0, 4.0)	0.000
24 weeks, kg	6.0 (4.5, 7.85)	7.0 (5.0, 8.0)	6.0 (4.6, 8.0)	5.5 (3.9, 7.5)	4.9 (3.0, 6.5)	0.000
28 weeks, kg	8.5 (6.5, 10.5)	9.0 (7.0, 11.0)	9.0 (7.0, 10.5)	7.9 (6.0, 10.0)	6.1 (4.4, 8.7)	0.000
Z-score						
16 weeks	–0.16 (–0.82, 0.47)	–0.14 (–0.82, 0.42)	–0.18 (–0.75, 0.42)	–0.17 (–0.97, 0.49)	0.01 (–0.78, 0.7)	0.204
20 weeks	0.14 (–0.58, 0.68)	0.17 (–0.47, 0.64)	0.11 (–0.58, 0.68)	0.17 (–0.58, 0.73)	0.13 (–0.78, 0.85)	0.506
24 weeks	0.08 (–0.61, 0.7)	0.10 (–0.6, 0.61)	0.04 (–0.62, 0.7)	0.10 (–0.63, 0.72)	0.18 (–0.57, 0.78)	0.779
28 weeks	0.10 (–0.52, 0.7)	0.09 (–0.59, 0.71)	0.13 (–0.43, 0.68)	0.06 (–0.59, 0.71)	0.05 (–0.65, 0.72)	0.726

HDP – hypertensive disorders during pregnancy; Han ethnicity – the ethnic majority in China; BMI – body mass index; GW – gestational week; GWG – gestational weight gain.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 2. Descriptive characteristics of pregnancies with and without HDP in different early-pregnancy BMI categories.

Characteristic	Total (N=5295)			Underweight (N=512)			Normal weight (N=3231)		
	CG	HDP	P	CG	HDP	P	CG	HDP	P
Sample	N=5010, 94.6%	N=285, 5.4%		N=500, 97.7%	N=12, 2.3%		N=3118, 96.5%	N=113, 3.5%	
Age, y	30 (28, 33)	31 (28, 34)	0.075	29 (27, 31)	28 (27, 30)	0.524	30 (28, 33)	29 (28, 34)	0.915
Ethnicity (Han)	4803 (95.9%)	281 (98.6%)	**0.022**	482 (96.4%)	12 (100%)	1.000	2982 (95.6%)	111 (98.2%)	0.271
Primipara	3438 (68.6%)	218 (76.5%)	**0.005**	404 (80.8%)	10 (83.3%)	1.000	2151 (69.0%)	96 (85.0%)	**0.000**
FH of hypertension	911 (18.2%)	84 (29.5%)	**0.000**	81 (16.2%)	1 (8.3%)	0.737	538 (17.3%)	33 (29.2%)	**0.001**
BMI at enrolment, kg/m^2	21.8 (19.9, 24.3)	24.9 (21.7, 27.2)	**0.000**	17.7 (17.1, 18.2)	18 (17, 18.1)	0.697	21.1 (19.9, 22.3)	21.6 (20.3, 22.9)	**0.018**
GW at enrolment, week	11^{+0} (9^{+5}, 12^{+1})	11^{+0} (9^{+5}, 12^{+0})	0.851	11^{+1} (10^{+0}, 12^{+2})	10^{+4} (10^{+0}, 11^{+5})	0.399	11^{+0} (9^{+5}, 12^{+1})	10^{+4} (9^{+2}, 11^{+6})	0.078
GW at delivery, week	39^{+3} (38^{+4}, 40^{+1})	38^{+5} (37^{+5}, 39^{+6})	**0.000**	39^{+3} (38^{+6}, 40^{+1})	39^{+6} (38^{+4}, 40^{+4})	0.429	39^{+3} (38^{+4}, 40^{+2})	38^{+5} (37^{+5}, 39^{+6})	**0.000**
Caesarean section	2527 (50.4%)	193 (67.7%)	**0.000**	173 (34.6%)	5 (41.7%)	0.840	1470 (47.1%)	72 (63.7%)	**0.001**
Neonatal sex (Male)	2658 (53.1%)	149 (52.3%)	0.799	258 (51.6%)	6 (50.5%)	0.913	1627 (52.2%)	55 (48.7%)	0.463
Neonatal height, cm	50 (50, 51)	50 (48, 50)	**0.000**	50 (49, 50)	50 (46, 51)	0.671	50 (50, 51)	50 (48, 50)	**0.000**
Neonatal weight, g	3360 (3084, 3650)	3200 (2835, 3535)	**0.000**	3220 (2980, 3450)	3165 (2938, 3455)	0.763	3350 (3070, 3620)	3130 (2715, 3500)	**0.000**
Neonatal score	10 (9, 10)	10 (9, 10)	**0.035**	10 (9, 10)	9 (9, 10)	0.080	10 (9, 10)	9 (9, 10)	**0.006**
Education level, years									
≤9	885 (17.3%)	44 (15.4%)	0.472	87 (20.5%)	0 (0.0%)	/	472 (15.1%)	18 (15.9%)	0.751
9 to 12	3595 (71.8%)	214 (75.1%)		364 (68.7%)	11 (91.7%)		2270 (72.8%)	84 (74.3%)	
>12	550 (11.0%)	27 (9.5%)		49 (10.8%)	1 (8.3%)		376 (12.1%)	11 (9.7%)	
GWG, kg									
16 weeks	1.0 (0.25, 2.0)	1.0 (0.0, 2.3)	0.991	1.5 (0.50, 2.5)	1.3 (0.7, 3.6)	0.930	1.0 (0.5, 2.0)	1.3 (0.5, 2.5)	0.447
20 weeks	3.5 (2.3, 5.0)	3.5 (2.0, 4.7)	0.147	4.0 (3.0, 5.5)	3.9 (2.8, 6.5)	0.957	3.8 (2.5, 5.0)	4.0 (2.5, 5.5)	0.338
24 weeks	6.0 (4.5, 7.9)	6.0 (4, 7.5)	0.381	7.0 (6.2, 9.4)	7.5 (6.2, 9.4)	0.218	6.0 (4.6, 8.0)	6.75 (5.0, 8.1)	**0.048**
28 weeks	8.5 (6.5, 10.5)	8.0 (6.0, 10.5)	0.555	9 (7.0, 11.0)	10.8 (9.4, 14.4)	0.045	8.9 (7.0, 10.5)	9.1 (7.1, 11.3)	**0.019**
Z-score around 16 weeks	–0.16 (–0.82, 0.45)	–0.16 (–0.77, 0.63)	0.124	–0.14 (–0.82, 0.39)	–0.30 (–0.71, 0.79)	0.876	–0.20 (–0.77, 0.36)	–0.16 (–0.75, 0.63)	0.257
<–1 SD	9.6%	11.0%	0.205	10.4%	10.0%	/	9.4%	11.9%	0.092
–1 to +1 SD	81.8%	77.6%		78.1%	70.0%		81.4%	73.3%	
>+1 SD	8.6%	11.4%		11.5%	20.0%		9.2%	14.9%	

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 2 continued. Descriptive characteristics of pregnancies with and without HDP in different early-pregnancy BMI categories.

Characteristic	Total (N=5295)			Underweight (N=512)			Normal weight (N=3231)		
	CG	HDP	P	CG	HDP	P	CG	HDP	P
Z-score around 20 weeks	0.13 (–0.58, 0.68)	0.21 (–0.48, 0.71)	0.373	0.17 (–0.47, 0.64)	0.22 (–0.48, 0.83)	0.878	0.08 (–0.58, 0.68)	0.23 (–0.43, 0.88)	0.088
<–1 SD	10.9%	8.6%		12.6%	9.1%		10.8%	8.4%	
–1 to +1 SD	78.9%	80.1%	0.468	74.6%	72.7%	/	78.5%	72.9%	**0.031**
>+1 SD	10.2%	11.2%		12.8%	18.2%		10.7%	18.7%	
Z-score around 24 weeks	0.08 (–0.61, 0.69)	0.23 (–0.52, 0.76)	0.223	0.05 (–0.60, 0.61)	0.31 (0.01, 0.96)	0.237	0.04 (–0.62, 0.70)	0.33 (–0.43, 0.81)	0.061
<–1 SD	12.7%	9.4%		12.4%	16.7%		14.0%	11.9%	
–1 to +1 SD	75.1%	79.5%	0.195	71.4%	58.3%	/	72.3%	67.0%	0.087
>+1 SD	12.2%	11.2%		16.1%	25.0%		13.7%	21.1%	
Z-score around 28 weeks	0.10 (–0.53, 0.70)	0.26 (–0.42, 0.84)	**0.049**	0.09 (–0.63, 0.71)	0.63 (0.18, 1.50)	0.038	0.13 (–0.43, 0.66)	0.31 (–0.30, 0.99)	**0.011**
<–1 SD	13.1%	11.2%		14.8%	8.3%		13.3%	10.7%	
–1 to +1 SD	73.6%	72.3%	0.222	69.5%	50.0%	/	73.7%	67.0%	**0.015**
>+1 SD	13.2%	16.5%		15.8%	41.7%		12.9%	22.3%	

CG – control group; HDP – hypertensive disorder during pregnancy; Han ethnicity – the ethnic majority in china; FH – family history; BMI – body mass index; GW – gestational week; GWG – gestational weight gain; SD – standard deviation.

Table 3. Descriptive characteristics of pregnancies with and without HDP in different early-pregnancy BMI categories.

Characteristic	Overweight n=1156			Obese n=396		
	CG	HDP	P	CG	HDP	P
Sample	N=1048, 90.7%	N=108, 9.3%		N=344, 86.9%	N=52, 13.1%	
Age, years	31 (29, 34)	31 (28, 34)	0.973	31 (29, 34)	32 (29, 35)	0.159
Ethnicity (Han)	1005 (95.9%)	107 (99.1%)	0.168	334 (97.1%)	51 (98.1%)	1.000
Primipara	663 (63.3%)	76 (70.4%)	0.143	220 (64.0%)	36 (69.2%)	0.458
FH of hypertension	210 (20.0%)	38 (23.2%)	**0.000**	82 (23.8%)	12 (23.1%)	0.904
BMI at enrolment kg/m^2	25.4 (24.6, 26.4)	25.9 (25.1, 26.9)	**0.001**	29.9 (28.7, 31.3)	30.5 (29, 31.9)	0.235
GW at enrolment weeks	10^{+6} (9^{+5}, 12^{+1})	11^{+3} (10^{+4}, 12^{+3})	**0.013**	11^{+2} (9^{+5}, 12^{+1})	10^{+6} (9^{+5}, 11^{+6})	0.318
GW at delivery, weeks	39^{+} (38^{+3}, 40^{+1})	38^{+5} (37^{+4}, 39^{+6})	**0.004**	39^{+0} (38^{+3}, 39^{+6})	39^{+0} (37^{+4}, 39^{+5})	0.152
Caesarean section	624 (59.5%)	81 (75.0%)	**0.002**	260 (75.6%)	35 (67.3%)	0.202
Neonatal sex (male)	571 (54.5%)	58 (53.7%)	0.877	202 (58.7%)	30 (57.7%)	0.888
Neonatal height, cm	50 (50, 51)	50 (48, 50)	**0.000**	50 (50, 51)	50 (49, 50)	**0.018**
Neonatal weight, g	3450 (3170, 3750)	3250 (2843, 3598)	**0.000**	3503 (3200, 3850)	3260 (3028, 3675)	**0.005**

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 3 continued. Descriptive characteristics of pregnancies with and without HDP in different early-pregnancy BMI categories.

Characteristic	Overweight n=1156			Obese n=396		
	CG	HDP	P	CG	HDP	P
Neonatal score	10 (9, 10)	10 (9, 10)	0.840	10 (9, 10)	10 (9, 10)	0.448
Education level, years						
≤9	209 (19.9%)	15 (13.9%)		97 (28.2%)	11 (21.2%)	
9 to 12	734 (70.0%)	82 (75.9%)	0.311	227 (66.0%)	37 (71.2%)	0.521
>12	105 (10.0%)	11 (10.2%)		20 (5.8%)	4 (7.7%)	
GWG, kg						
16 weeks	1.0 (0, 2)	1.3 (0.2, 2.3)	0.069	1.0 (0.0, 2.0)	0.5 (–1, 2.3)	0.448
20 weeks	3.3 (2.0, 4.9)	3.5 (2.0, 4.3)	0.963	2.5 (1.0, 4.3)	2.3 (0, 3.9)	0.270
24 weeks	5.5 (3.8, 7.5)	5.2 (4.0, 7.3)	0.961	5.0 (3.0, 6.5)	4.5 (2.1, 6.8)	0.541
28 weeks	8.0(6.0, 10.0)	7.8(6.0, 10.0)	0.876	6.3 (4.0, 8.8)	6.0 (5.0, 8.3)	0.929
Z-score around 16 weeks	–0.17 (–0.97, 0.45)	0.02 (–0.54, 0.74)	**0.014**	0.01 (–0.77, 0.70)	–0.36 (–1.90, 0.62)	**0.042**
<–1 SD	10.5%	4.3%		8.3%	21.6%	
–1 to +1 SD	84.0%	84.9%	**0.026**	83.8%	74.5%	**0.010**
>+1 SD	5.5%	10.8%		7.9%	3.9%	
Z-score around 20 weeks	–0.06±1.43; 0.17 (–0.58, 0.78)	0.07±0.88; 0.17 (–0.29, 0.63)	0.815	–0.14 (1.77); 0.18 (–0.65, 0.88)	–0.27 (1.39); 0.04 (–1.39, 0.62)	0.302
<–1 SD	10.9%	5.9%		8.9%	14.6%	
–1 to +1 SD	80.5%	89.1%	0.105	84.8%	79.2%	0.459
>+1 SD	8.7%	5.0%		6.3%	6.3%	
Z-score around 24 weeks	0.10 (–0.63, 0.72)	0.05 (–0.58, 0.69)	0.943	0.20 (–0.56, 0.78)	0.02 (–0.74, 0.81)	0.730
<–1 SD	10.4%	7.5%		7.9%	5.9%	
–1 to +1 SD	81.6%	89.6%	0.083	86.1%	90.2%	0.720
>+1 SD	8.0%	2.8%		6.0%	3.9%	
Z-score around 28 weeks	0.06 (–0.59, 0.74)	0.17 (–0.50, 0.61)	0.887	0.04 (–0.66, 0.72)	0.05 (–0.38, 0.68)	0.799
<–1 SD	12.2%	12.4%		11.4%	10.2%	
–1 to +1 SD	74.0%	77.1%	0.635	78.0%	79.6%	0.962
>+1 SD	13.8%	10.5%		10.5%	10.2%	

CG – control group; HDP – hypertensive disorder during pregnancy; Han ethnicity – the ethnic majority in china; FH – family history; BMI – body mass index; GW – gestational week; GWG – gestational weight gain; SD – standard deviation.

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 4. Relationship between weight gain, weight gain z-scores before the third trimester, and the risk of HDP.

		Underweight		Normal weight	
		Crude RR (95% CI)	Adjust RR (95% CI)	Crude RR (95% CI)	Adjust RR (95% CI)
16 weeks					
GWG		1.04 (0.69, 1.57)	1.03 (0.69, 1.55)	1.08 (0.93, 1.21)	1.08 (0.96, 1.21)
Z-score	Continuous	0.91 (0.58, 1.45)	0.93 (0.61, 1.43)	1.09 (0.93, 1.27)	1.08 (0.93, 1.27)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	0.93 (0.12, 7.40)	0.93 (0.12, 7.09)	0.72 (0.40, 1.31)	0.70 (0.39, 1.28)
	>+1 SD	1.78 (0.16, 19.00)	1.66 (0.15, 18.12)	1.26 (0.60, 2.64)	1.27 (0.60, 2.67)
20 weeks					
GWG		1.02 (0.76, 1.39)	1.01 (0.75, 1.37)	1.06 (0.97, 1.16)	1.06 (0.96, 1.15)
Z score	Continuous	0.83 (0.48, 1.44)	0.82 (0.47, 1.44)	1.14 (0.95, 1.37)	1.12 (0.93, 1.34)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	1.34 (0.17, 10.53)	1.39 (0.18, 10.61)	1.19 (0.60, 2.34)	1.10 (0.56, 2.18)
	>+1 SD	1.94 (0.18, 20.79)	1.88 (0.18, 19.51)	2.17 (1.00, 4.69)*	2.06 (0.95, 4.47)
24 weeks					
GWG		1.11 (0.88, 1.39)	1.10 (0.88, 1.37)	1.08 (1.01, 1.16)*	1.07 (0.99, 1.15)
Z score	Continuous	1.15 (0.60, 2.18)	1.12 (0.60, 2.10)	1.22 (1.00, 1.48)*	1.19 (0.98, 1.44)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	0.62 (0.13, 2.90)	0.65 (0.14, 3.00)	1.086 (0.61, 1.94)	1.03 (0.58, 1.82
	>+1 SD	1.15 (0.20, 6.66)	1.16 (0.19, 7.00)	1.76 (0.91, 3.45)	1.62 (0.83, 3.16)
28 weeks					
GWG		1.23 (1.02, 1.47)*	1.21 (1.01, 1.45)*	1.09 (1.02, 1.15)**	1.08 (1.02, 1.15)**
Z score	Continuous	1.74 (0.89, 3.38)	1.68 (0.87, 3.25)	1.30 (1.06, 1.60)*	1.29 (1.05, 1.58)*
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	1.27 (0.16, 10.39)	1.27 (0.15, 10.20)	1.13 (0.62, 2.06)	1.12 (0.62, 2.04)
	>+1 SD	4.45 (0.53, 37.22)	4.17 (0.46, 37.76)	2.08 (1.06, 4.09)*	2.08 (1.06, 4.08)*
		Overweight		**Obesity**	
		Crude RR (95% CI)	**Adjust RR (95% CI)**	**Crude RR (95% CI)**	**Adjust RR (95% CI)**
16 weeks					
GWG		1.12 (1.01, 1.25)*	1.12 (1.01, 1.25)*	0.90 (0.79, 1.02)	0.89 (0.78, 1.02)
Z-score	Continuous	1.31 (1.10, 1.60)**	1.32 (1.09, 1.57)**	0.90 (0.82, 0.99)*	0.89 (0.81, 0.98)*
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	2.34 (0.87, 6.25)	2.23 (0.81, 6.10)	0.42 (0.24, 0.75)**	0.36 (0.20, 0.65)**
	>+1 SD	4.19 (1.37, 12.80)*	4.21 (1.36, 13.01)*	0.25 (0.06, 1.03)	0.22 (0.05, 0.90)*
20 weeks					
GWG		1.00 (0.92, 1.08)	1.00 (0.92, 1.08)	0.94 (0.85, 1.04)	0.94 (0.85, 1.03)
Z score	Continuous	1.07 (0.92, 1.25)	1.07 (0.92, 1.25)	0.97 (0.85, 1.10)	0.96 (0.84, 1.09)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	1.92 (0.86, 4.29)	1.84 (0.82, 4.13)	0.62 (0.30, 1.29)	0.59 (0.28, 1.22)
	>+1 SD	1.04 (0.33, 3.31)	1.08 (0.33, 3.49)	0.65 (0.19, 2.27)	0.63 (0.17, 2.32)

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

Table 4 continued. Relationship between weight gain, weight gain z-scores before the third trimester, and the risk of HDP.

		Overweight		Obesity	
		Crude RR (95% CI)	Adjust RR (95% CI)	Crude RR (95% CI)	Adjust RR (95% CI)
24 weeks					
GWG		0.99 (0.93, 1.05)	0.99 (0.93, 1.06)	0.97 (0.90, 1.06)	0.98 (0.90, 1.07)
Z score	Continuous	0.97 (0.86, 1.09)	0.97 (0.86, 1.10)	0.97 (0.86, 1.10)	0.98 (0.86, 1.11)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	1.46 (0.73, 2.93)	1.31 (0.65, 2.62)	1.34 (0.45, 4.05)	1.38 (0.47, 4.11)
	>+1 SD	0.50 (0.14, 1.84)	0.49 (0.14, 1.76)	0.88 (0.16, 4.82)	0.93 (0.17, 5.23)
28 weeks					
GWG		0.98 (0.93, 1.04)	0.99 (0.93, 1.05)	1.00 (0.93, 1.07)	1.01 (0.93, 1.08)
Z score	Continuous	0.97 (0.82, 1.14)	0.97 (0.81, 1.15)	1.06 (0.85, 1.31)	1.07 (0.85, 1.34)
	<–1 SD	Referent	Referent	Referent	Referent
	–1 to +1 SD	1.03 (0.59, 179)	1.02 (0.58, 1.81)	1.13 (0.47, 2.70)	1.19 (0.49, 2.90)
	>+1 SD	0.77 (0.36, 1.66)	0.80 (0.37, 1.72)	1.08 (0.34, 3.44)	1.19 (0.36, 3.93)

RR – relative risk; GWG – gestational weight gain; SD – standard deviation. * P<0.05; ** P<0.01.

(weight gain RR: 1.08, 95% CI: 1.02–1.15; weight gain z-score RR: 1.29, 95% CI: 1.05–1.58). Compared to the reference of low weight gain (<–1 SD), weight gain >+1 SD was associated with an approximately 2.0 times greater likelihood of HDP (RR: 2.08, 95% CI: 1.06–4.08). Weight gain and weight gain z-scores at the remaining time points were not related to the risk of HDP, and the relationships among the other periods were not significant. Among the overweight women, weight gain and weight gain z-scores at approximately 16 weeks were associated with an increased risk of HDP (weight gain RR: 1.12, 95% CI: 1.01–1.25; weight gain z-score RR: 1.32, 95% CI: 1.09–1.57). Compared to the reference of low weight gain (<–1 SD), weight gain >+1 SD at approximately 16 weeks significantly increased the risk of developing HDP (RR: 4.21, 95% CI: 1.36–13.01), while in obese women, there was a negative relationship between weight gain at approximately 16 weeks and the risk of HDP. Associations were null for the other periods.

Discussion

This study supports that an increase in early-pregnancy BMI increases the risk of HDP and that primiparous women and pregnant women with a family history of hypertension have higher risks of HDP [16–18]. There was a positive relationship between weight gain at approximately 28 weeks and the risk of HDP among women with early-pregnancy underweight and normal weight. Even adjusted for recognized high-risk factors of HDP, such as age, early pregnancy BMI, primipara, and family history of hypertension, the relationship remained in the normal-weight group. There was no significant difference in weight gain at 20-24 weeks in each group and 20-28 weeks in the overweight and obese group.

Due to methodological problems associated with the use of total GWG as the exposure as opposed to a weight gain before the diagnosis of HDP, the results of published studies on the association between GWG and HDP remains inconsistent and inconclusive [9]. The present study is one of the few studies investigating the effect of GWG before the third trimester on hypertension disorders. A smaller-cohort study (n=1441) from the United States found that women with weight gain in the first 28 weeks above the Institute of Medicine (IOM) recommendation were more likely to develop HDP [19]. Our results were also consistent with those of a recently published population-based cohort study in Sweden (n=62 705), which showed that weight gain between women with and without preeclampsia did not differ until week 25 in normal-weight women and week 30 in obese women, and the higher the early pregnancy BMI, the higher the gestational age when weight gain trajectories of women with and without preeclampsia diverged [10]. The mechanisms underlying the association between pregnancy weight and HDP have not been fully explained, but may involve insulin resistance, inflammation, oxidative stress, and dyslipidemia. Obesity and excessive weight gain during pregnancy can promote endothelial and vascular dysfunction, which can predispose women to HDP [20].

Our study was observational and thus could not demonstrate whether weight gain was the cause of HDP or the accompanying symptoms of the disease. Therefore, whether an intervention in weight change during pregnancy could reduce the

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

incidence of HDP remains undetermined, but considering that the mean gestational age at which blood pressure began to increase in women with HDP was approximately 34 weeks in the study, we suggest that pregnant women with an early pregnancy BMI <24 kg/m^2, especially a BMI of 18.5–23.9 kg/m^2 but excessive weight gain at approximately 28 gestational weeks, should be closely monitored to reduce complications in the mother and infant.

The difference in weight gain at approximately 16 weeks between women with and without HDP was not obvious in the underweight and normal-weight groups in this Chinese cohort study. Among the overweight women, weight gain at 16 weeks in women with HDP was higher than that of women without HDP. Unexpectedly, the result was reversed in the obese group.

The results of studies on weight gain in early pregnancy and the risk of HDP are inconsistent. One cohort study from China (n=84 656) showed that compared to weight gain of <200 g/week up to 18 weeks gestation, the highest level of weight gain (≥600 g/week) significantly increased the risk of developing HDP among pre-pregnancy normal-weight and overweight/obese women [21]. Another cohort study (n=80 812) showed that, compared with a weight gain of 1.2 kg, a weight gain of 7.2 kg at 16–19 weeks steadily increased the risk of preeclampsia in pre-pregnancy women with normal weight and grade 2 or 3 obesity, and associations were null in overweight women and women with grade 1 obesity [11]. A cohort study in Sweden suggested that early-pregnancy weight gain in various BMI groups was not associated with the risk of HDP [10]. Our study showed a positive correlation between weight gain in early pregnancy and the risk of HDP in overweight women in early pregnancy but not in normal-weight or underweight women. The inconsistency of these research results may have been related to the different starting points of these studies. The first 2 studies used pre-pregnancy weight as the starting point, while the latter 2 studies used the weight at less than 14 weeks of gestation (the average gestational age was approximately 9–11 weeks). Insufficient time intervals may lead to insignificant weight differences. However, weight gain in such a short period in overweight women in our study was related to an increased risk of HDP, which still justifies our attention to weight gain in early pregnancy. The contradictory performance in early pregnancy in obese women may be related to the small sample size of obese women in our study (n=396), individual differences (such as weight fluctuations due to vomiting during early pregnancy), focused education for obese pregnant women by medical staff [22], and the complex pathophysiological mechanism of preeclampsia (such as placental dysfunction in early gestation and a decrease in the normal expansion in maternal intravascular volume, which can affect the weight gain of women in early gestation) [9].

In summary, the association between increased GWG in early pregnancy and HDP was less clear, and it was still necessary to pay attention to the effects of early-pregnancy weight gain on HDP, using pre-pregnancy weight for assessment, if possible.

The present study showed that with the increase in early-pregnancy BMI, the mean weight gain during each gestational period gradually decreased, but there was no difference in weight gain z-score between the 4 BMI groups, as the z-score was calculated according to the mean and standard deviation of the weight gain per gestational week of healthy women with full-term pregnancies in each BMI group, which demonstrated the Z-score was BMI-specific. In each BMI group there was a consistent tendency for weight gain and weight gain z-score in evaluating weight gain and HDP risk, except for a slight difference in the statistical conclusion, such as weight gain at approximately 16 weeks in the obese group.

To date, few studies have investigated the relationship between weight gain and the risk of HDP using z-scores [10,11]. A case-control study showed that early-pregnancy weight gain z-score was associated with preeclampsia risk in some subgroups and did not assess the consistency of weight gain and the weight gain z-score [11]. Another study, performed in Stockholm-Gotland, showed that for every 1 z-score increase in weight gain before diagnosis, the risk of preeclampsia increased by nearly 60% in normal-weight and overweight women and by 20% in obese women. The study estimated weight gain (kg) trajectories of women with and without preeclampsia, confirming that the weight gain z-score before diagnosis was consistent with the weight gain trajectory [10]. Our research showed that weight gain z-score was not more sensitive than weight gain value in analyzing the relationship between weight gain before the third trimester and HDP risk. Considering that z-scores can theoretically eliminate the confounding bias of gestational duration on GWG, the result may be related to the pregnancy periods observed in our research rather than a methodological issue. Z-score may be more advantageous in analyzing the relationship between GWG before disease diagnosis or delivery (mostly after the third trimester), which is related to the duration of pregnancy, and HDP risk.

Research limitations

First, our study population was located in 19 communities in Tianjin, and the resident population is mostly of Han ethnicity. Therefore, this study can only represent the characteristics of the Han population in northern China. Second, considering the low incidence of HDP, the overall population of the study was not large, especially for the underweight and obese women, so the research data in these 2 groups were not sufficiently accurate. Third, some studies have shown that the relationship between weight gain and the risk of HDP subtypes

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]

was not the same. The present study did not analyze this relationship because of the number of people enrolled. Results are still being collated, and future large-sample cohort studies may provide a sufficient number of cases for analysis. Finally, using early-pregnancy BMI as the basis for grouping may have caused bias in enrolment. However, the pre-pregnancy weight mainly depended on the memory of the pregnant woman, and there may be recall errors. The grouping basis of the z-score chart in the Chinese population that our study represented is the early-pregnancy BMI, and the sensitivity analyses in the study indicated that the possibility of misclassification was small and acceptable [14].

Conclusions

Excessive weight gain before the third trimester, independent of age, early pregnancy BMI, primipara, and family history of hypertension, was associated with a greater risk of developing HDP among women with early-pregnancy normal weight, which may provide a chance to identify subsequent hypertensive disorders. The relationship between weight gain in early pregnancy and the risk of HDP remains unclear. Additional large-sample research with serial antenatal weight measure (including pre-pregnancy weight) are need to determine whether early-pregnancy weight gain is associated with HDP risk.

Acknowledgments

The authors thank all the participants who contributed their data and all hospitals involved in this study.

Conflicts of interest

None.

References:

1. Garovic VD, Bailey KR, Boerwinkle E et al: Hypertension in pregnancy as a risk factor for cardiovascular disease later in life. J Hypertens, 2010; 28(4): 826–33
2. Bergen NE, Schalekamp-Timmermans S, Roos-Hesselink J et al: Hypertensive disorders of pregnancy and subsequent maternal cardiovascular health. Eur J Epidemiol, 2018; 33(8): 763–71
3. Leon LJ, McCarthy FP, Direk K et al: Preeclampsia and cardiovascular disease in a large UK pregnancy cohort of linked electronic health records: A caliber study. Circulation, 2019; 140(13): 1050–60
4. Herrera-Garcia G, Contag S: Maternal preeclampsia and risk for cardiovascular disease in offspring. Curr Hypertens Rep, 2014; 16(9): 475
5. Wang AM, Karumanchi SA: Offspring ardiovascular disease in preeclampsia: Nature versus nurture? Hypertension (Dallas, TX: 1979), 2017; 69(4): 589–90
6. Cedergren M: Effects of gestational weight gain and body mass index on obstetric outcome in Sweden. Int J Gynaecol Obstet, 2006; 93(3): 269–74
7. Poston L, Harthoorn LF, Van Der Beek EM: Obesity in pregnancy: Implications for the mother and lifelong health of the child. A consensus statement. Pediatr Res, 2011; 69(2): 175–80
8. Spradley FT, Palei AC, Granger JP: Increased risk for the development of preeclampsia in obese pregnancies: Weighing in on the mechanisms. Am J Physiol Regul Integr Comp Physiol, 2015; 309(11): R1326–43
9. Institute of Medicine (US), National Research Council (US) Committee to Reexamine IOM Pregnancy Weight Guidelines. In: The National Academies Collection: Reports funded by National Institutes of Health. Rasmussen KM, Yaktine AL (eds.), Weight gain during pregnancy: Reexamining the guidelines. Washington (DC): National Academies Press (US). National Academy of Sciences, 2009
10. Hutcheon JA, Stephansson O, Cnattingius S et al: Pregnancy weight gain before diagnosis and risk of preeclampsia: A population-based cohort study in nulliparous women. Hypertension (Dallas, TX: 1979), 2018; 72(2): 433–41
11. Bodnar LM, Himes KP, Abrams B et al: Early-pregnancy weight gain and the risk of preeclampsia: A case-cohort study. Pregnancy Hypertens, 2018; 14: 205–12
12. Bodnar LM, Hutcheon JA, Parisi SM et al: Comparison of gestational weight gain z-scores and traditional weight gain measures in relation to perinatal outcomes. Paediatr Perinat Epidemiol, 2015; 29(1): 11–21
13. Hutcheon JA, Bodnar LM, Joseph KS et al: The bias in current measures of gestational weight gain. Paediatr Perinat Epidemiol, 2012; 26(2): 109–16
14. Huang A, Xiao Y, Hu H et al: Gestational weight gain charts by gestational age and body mass index for Chinese women: A population-based follow-up study. J Epidemiol, 2020; 30(8): 345–53
15. Hypertensive Disorders in Pregnancy Subgroup, Chinese Society of Obstetrics and Gynecology, Chinese Medical Association; Hypertensive Disorders in Pregnancy Subgroup Chinese Society of Obstetrics and Gynecology Chinese Medical Association: [Diagnosis and treatment guideline of hypertensive disorders in pregnancy (2015)]. Zhonghua Fu Chan Ke Za Zhi, 2015; 50(10): 721–28
16. Bezerra PC, Leão MD, Queiroz JW et al: Family history of hypertension as an important risk factor for the development of severe preeclampsia. Acta Obstet Gynecol Scand, 2010; 89(5): 612–17
17. Bartsch E, Medcalf KE, Park AL, Ray JG: Clinical risk factors for pre-eclampsia determined in early pregnancy: Systematic review and meta-analysis of large cohort studies. BMJ, 2016; 353: i1753
18. Voerman E, Santos S, Inskip H et al: Association of gestational weight gain with adverse maternal and infant outcomes. JAMA, 2019; 321(17): 1702–15
19. Ruhstaller KE, Bastek JA, Thomas A et al: The effect of early excessive weight gain on the development of hypertension in pregnancy. Am J Perinatol, 2016; 33(12): 1205–10
20. Spradley FT: Metabolic abnormalities and obesity's impact on the risk for developing preeclampsia. Am J Physiol Regul Integr Comp Physiol, 2017; 312(1): R5–12
21. Zhou A, Xiong C, Hu R et al: Pre-pregnancy BMI, gestational weight gain, and the risk of hypertensive disorders of pregnancy: A cohort study in Wuhan, China. PLoS One, 2015; 10(8): e0136291
22. Ma RCW, Schmidt MI, Tam WH et al: Clinical management of pregnancy in the obese mother: Before conception, during pregnancy, and post partum. Lancet Diabetes Endocrinol, 2016; 4(12): 1037–49

Indexed in: [Current Contents/Clinical Medicine] [SCI Expanded] [ISI Alerting System] [ISI Journals Master List] [Index Medicus/MEDLINE] [EMBASE/Excerpta Medica] [Chemical Abstracts/CAS]