Original Article

Prehypertension During Normotensive Pregnancy and Postpartum Clustering of Cardiometabolic Risk Factors

A Prospective Cohort Study

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Abstract—The nonstratification of blood pressure (BP) levels may underestimate future cardiovascular risk in pregnant women who present with BP levels in the range of prehypertension (120–139/80–89 mm Hg). We prospectively evaluated the relationship between multiple antepartum BP measurements (from 11^{+0} to 13^{+6} weeks' gestation to term) and the occurrence of postpartum metabolic syndrome in 507 normotensive pregnant women after a live birth. By using latent class growth modeling, we identified the following 3 distinctive diastolic BP (DBP) trajectory groups: the low-J-shaped group (34.2%; DBP from 62.5±5.8 to 65.0±6.8 mm Hg), the moderate-U-shaped group (52.6%; DBP from 71.0±5.9 to 69.8±6.2 mm Hg), and the elevated-J-shaped group (13.2%; DBP from 76.2±6.7 to 81.8±4.8 mm Hg). Notably, the elevated-J-shaped trajectory group had mean DBP and systolic BP levels within the range of prehypertension from 37^{+0} and 26^{+0} weeks of pregnancy, respectively. Among the 309 women who completed the ≈1.6 years of postpartum follow-up, the women in the elevated-J-shaped group had greater odds of developing postpartum metabolic syndrome (adjusted odds ratio, 6.55; 95% confidence interval, 1.79–23.92; P=0.004) than the low-J-shaped group. Moreover, a parsimonious model incorporating DBP (membership in the elevated-J-shaped group but not in the DBP prehypertension group as identified by a single measurement) and elevated levels of fasting glucose (>4.99 mmol/L) and triglycerides (>3.14 mmol/L) at term was developed, with good discrimination and calibration for postpartum metabolic syndrome (c-statistic, 0.764; 95% confidence interval, 0.674–0.855; P<0.001). Therefore, prehypertension identified by DBP trajectories throughout pregnancy is an independent risk factor for predicting postpartum metabolic syndrome in normotensive pregnant women. **(*Hypertension*. 2016;68:00-00. DOI: 10.1161/HYPERTENSIONAHA.116.07261.)** ● **Online Data Supplement**

Key Words: blood pressure ■ cohort studies ■ metabolic syndrome X ■ pregnancy ■ prehypertension

As a result of biphasic changes in peripheral arterial resistance during pregnancy, the blood pressure (BP) level undergoes a gradual decrease to the nadir at midpregnancy and returns to a prepregnant level through term.[1,2] Consequently, this physiological alteration leads to the question of whether the criteria for the diagnosis of gestational hypertension are suitable because the current criteria (systolic BP [SBP] ≥140 mm Hg and diastolic BP [DBP] ≥90 mm Hg) are derived from the nonpregnant population. The optimal BP levels in pregnant women remain an open question.

Emerging evidence shows that prehypertension (120–139/80–89 mm Hg), defined by the seventh report of the Joint National Committee on Prevention,[3] not only increases the risk of incident hypertension but also is associated with an increased risk of cardiovascular disease (CVD).[4–7] Although prehypertension is not addressed by the eighth Joint National Committee on Prevention,[8] the diagnosis of prehypertension provides a unique understanding of when future CVD trajectories could be changed by lifestyle modifications.[4] Recent studies have demonstrated associations between prehypertension before pregnancy and hypertensive disorders during pregnancy and gestational diabetes mellitus.[9–11] To our knowledge, the association between prehypertension during pregnancy and postpartum cardiovascular risk has not been addressed.

Pregnancy is a known, long-term cardiovascular stress test for women. The presence of hypertensive disorders in pregnancy (HDP) is generally recognized as a maladaptation to pregnancy-induced hemodynamic and metabolic alterations.[12,13] In addition,

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women with HDP have a clustering of metabolic syndrome (MetS) traits during and after pregnancy,[14–17] which suggests that HDP, MetS, and future CVD are closely related.[15,18–20] Despite a consistent association between HDP and future cardiovascular risk,[21–23] the relationship between antepartum prehypertension and postpartum cardiometabolic risk is unclear. Therefore, in the present study, we examined the association between prehypertension during pregnancy and the postpartum occurrence of cardiometabolic risk clustering, ie, MetS, which is a surrogate marker of cardiovascular health, in a cohort of women with normotensive and uncomplicated pregnancies.

Methods

Study Cohort

This prospective cohort study was performed in a specialized hospital for women and children in Guangzhou, the third largest city in China. The aim of the study was to investigate the antepartum and postpartum health of women and fetuses/infants. Consecutive pregnant women were considered eligible if they met the following criteria: gestational age between 11^{+0} and 13^{+6} weeks, singleton pregnancy, normal BP levels (<140/90 mm Hg), normal glucose and lipid profiles, nonsmokers, no history of alcohol or substance abuse, and no history of vaginal bleeding. In addition, to maximize the follow-up rate, all participants had to be registered as permanent residents of Guangzhou. Informed consent was obtained from all participants in accordance with the Declaration of Helsinki, and the study was approved by the Hospital Ethics Committee. The study design and research flowchart are shown in Figure 1. A standardized questionnaire was completed for every participant through interviews and the review of patient medical records. The questionnaire contained demographic, medical, gynecological, obstetric and social history, as well as inquiries about body mass index before pregnancy, gestational weight gain, and the vital signs obtained during the physical examination. Obstetric measurements, ultrasound scans, and biochemical tests were also performed to ensure the medical health status of all participants and fetuses. At the end of the pregnancies, after excluding the patients with maternal and fetal abnormalities, the remaining participants with a live birth were enrolled for BP trajectory modeling (see Statistical Analysis section of this article) and postpartum follow-up.

Antepartum and Postpartum Check-Up

From 11^{+0} to 13^{+6} weeks of gestation (participant enrollment) until term, at least 7 antepartum visits were performed. The routine antepartum check-up included body weight, BP, and obstetric measurements and an ultrasound scan. All obstetric measurements were performed by well-trained midwives or obstetricians. There were no between-midwife variations in the mean values of the data collected, and the error rates were consistently <1% in the repeated data entry checks. The body weight and BP measurements (see below) were taken on the morning of each visit. Antepartum biochemical tests were conducted at the antenatal clinic visit closest to delivery (≥37^{+0} weeks).

The routine postpartum follow-up visit was performed within 6 to 12 weeks postpartum. In addition, a second follow-up visit was performed between May 1, 2011, and April 30, 2015 (0.5–3 years postpartum) to evaluate postpartum cardiometabolic risk. Body weight, BP, and waist circumference were measured.

Venous blood samples after an overnight fast were collected at baseline (gestational ages of 11^{+0}–13^{+6}), before term, and during the second postpartum follow-up to measure the levels of plasma glucose (FPG), insulin, total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides, low-density lipoprotein, and free fatty acids. Insulin resistance was assessed by the homeostatic model assessment (HOMA-IR).[24]

Definitions

To minimize variations in BP measurement, each subject was comfortably seated with his/her back supported for at least 10 minutes of rest, and then, a standard cuff for adults fitted with a mercury sphygmomanometer was used to check BP by a trained nurse. BP was measured on the right arm by placing the stethoscope bell lightly over the brachial artery and auscultating the Korotkoff sounds. BP was usually measured once. If BP was ≥140/90 mm Hg, a second measurement was performed after at least 5 minutes of rest, and the average of the 2 BP values was recorded. Hypertension was defined by an SBP ≥140 mm Hg and DBP ≥90 mm Hg on 3 visits or by current treatment with antihypertensive medications.

During the second postpartum follow-up, the following cardiometabolic risk factors were assessed in all participants: elevated waist circumference (≥80 cm, according to specific definition for Chinese women), elevated triglycerides level (≥1.7 mmol/L), decreased HDL-C level (<1.3 mmol/L), elevated FPG level (≥5.6 mmol/L), and elevated BP level (≥135/85 mm Hg).[25] MetS was defined as the clustering of ≥3 of the risk factors listed above.[25]

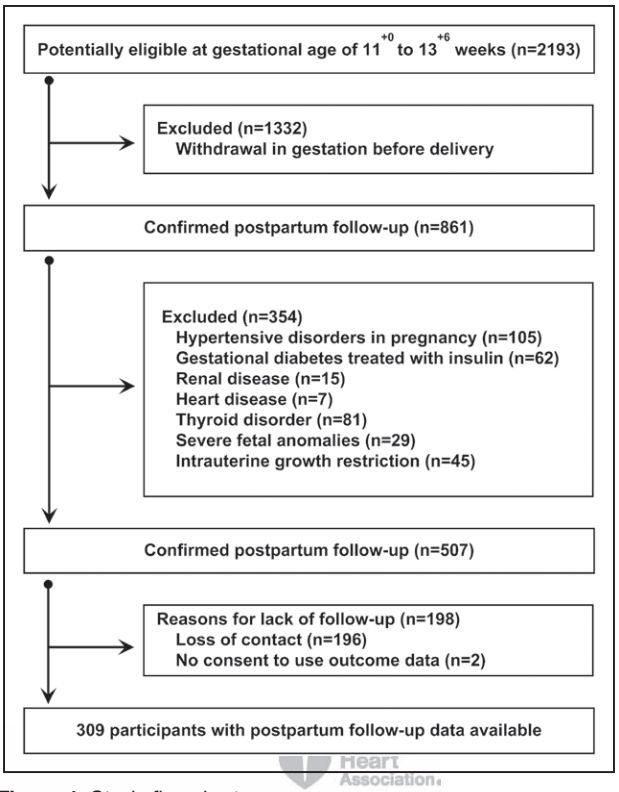

Figure 1. Study flowchart.

Statistical Analysis

To delineate the pattern of BP changes during pregnancy, we used latent class growth modeling to identify the distinctive subgroups that shared a similar underlying BP trajectory.[26] BP trajectories were modeled among the 507 uncomplicated, normotensive pregnant women, with the BP measurements obtained at the gestational ages of 11^{+0}–13^{+6}, 21^{+0}–24^{+6}, 25^{+0}–28^{+6}, 29^{+0}–32^{+6}, 33^{+0}–36^{+6}, 37^{+0}–38^{+6}, and 40^{+0} weeks during the routine obstetric examinations at the outpatient department. Only the participants who finished the second postpartum follow-up visit were included in the models examining the associations between BP indices and MetS. The STATA procedure traj, a new plugin for estimating group-based trajectory models that is similar to a well-established SAS-based procedure (Proc Traj),[27,28] was used for the analysis with a censored normal model that was appropriate for continuous, normally distributed data. The BP indices used for the modeling included DBP, SBP, mean arterial pressure (MAP), and mean mid-BP (calculated as [SBP+DBP]/2, a marker of coronary heart disease risk among younger populations).[29,30] The following criteria were used to determine the number of BP trajectory groups and the trajectory shapes for each BP index[31,32]: (1) an a priori

knowledge of BP development over time; (2) tendency toward a parsimonious model; (3) the difference between a simpler model and the more complex model by log Bayes Factor (higher values indicate stronger differences); and (4) each group had an average posterior probability of group membership >0.80.

Continuous variables with normal distributions are presented as the mean±SD or as medians with interquartile ranges if the data failed the normality test unless otherwise specified. Dichotomous data are presented as numbers and percentages. The differences between the groups were tested with Student *t* test, and categorical data were tested with the χ^2 test. Comparisons of continuous data with a skewed distribution were performed using the Mann–Whitney *U* test. To determine the association between BP trajectory membership of each BP index and postpartum MetS, a univariate logistic regression analysis was performed, followed by an adjustment for potential confounders that significantly differed between the MetS and the non-MetS participants. The κ statistic was used to assess the agreement between the BP trajectory-defined high-risk participants and the high-risk subjects identified by a single BP measurement at term. To construct prediction models for postpartum MetS using clinical variables at term, a receiver operator characteristic curve analysis was first used to assess the accuracy and the optimal cutoff value (the best Youden Index: sensitivity+specificity−1) of MetS-related parameters (FPG, triglycerides, HDL-C, SBP trajectories, SBP prehypertension exposure at term, SBP [as a continuous variable] at term, DBP trajectories, DBP prehypertension exposure at term, and DBP [as a continuous variable] at term) to discriminate between postpartum MetS and non-MetS participants. Subsequently, variables with a $P<0.1$ were included in the multivariate logistic regression model to identify the most parsimonious, clinically sound predictors of postpartum MetS. Internal validation of the prediction models was performed by bootstrapping, using 1000 random resamples from the entire data set. Model discrimination and calibration were performed using the *c*-statistic and the Hosmer–Lemeshow test, respectively. During the follow-up, univariate and multivariate linear regression analyses were used to establish associations between the value of the study parameters and BP levels. For all tests, a 2-tailed $P<0.05$ indicated statistical significance. Statistical analyses were performed using STATA version 14.1 (STATA Corp., College Station, TX).

Results

Initially, a total of 2193 normotensive pregnant women with an estimated delivery date between October 1, 2010, and September 30, 2012, were enrolled for further examinations. During the antepartum visits, 1332 women withdrew from the study, and another 354 women were excluded because of maternal and fetal abnormalities. Therefore, the postpartum follow-up was performed on 507 women with a live birth and complete data for all maternal characteristics; the BP trajectory modeling was also performed on these 507 women. A total of 311 participants finished the postpartum follow-up visit and had complete data available for analysis. After 2 participants were excluded because they did not consent to the use of the outcome data, 309 cases were analyzed, resulting in a follow-up rate of 60.9% (309/507). Notably, there was no self-reported smoking data for our cohort.

As shown in Table 1, among the 309 participants with follow-up data, 35 participants (11.3%) had MetS. Compared with non-MetS subjects, MetS participants had more advanced maternal age, elevated free fatty acids level before delivery, higher neonatal weight, and higher prepregnancy, term, and follow-up body mass index. In addition, the MetS participants were also characterized by a progressive deterioration of insulin resistance, with a nonsignificant elevation of HOMA-IR at baseline and at term, as well as a significant increase during follow-up.

To investigate the associations between pregnancy BP indices and postpartum MetS, we first modeled the DBP, SBP, MAP, and mid-BP trajectories during pregnancy in the 507 participants. For DBP, a 3-trajectory group model with quadratic specifications for all groups was identified. The 3 discrete trajectory lines, as well as the dynamic changes in DBP and SBP levels, are plotted in Figure 2. In this group model (Figure 2A), 32.4% of the participants maintained a low DBP level at 11^{+0} to 13^{+6} weeks, with a J-shaped change until term (group 1: herein referred to the low-J-shaped group; DBP from 62.5±5.8 mm Hg at gestational weeks of 11^{+0}–13^{+6} to 65.0±6.8 mm Hg at term), 52.5% of participants had a mean DBP level of ≈70 mm Hg at 11^{+0} to 13^{+6} weeks, with a slightly U-shaped change during pregnancy (group 2: the moderate-U-shaped group; DBP from 71.0±5.9 to 69.8±6.2 mm Hg), and 13.2% participants had an elevated baseline DBP level of ≈75 mm Hg, with a J-shaped change thereafter (group 3: the elevated-J-shaped group; DBP from 76.2±6.7 to 81.8±4.8 mm Hg). Notably, the elevated-J-shaped trajectory group had mean DBP and SBP levels within the range of prehypertension from 37^{+0} weeks and 26^{+0} weeks of pregnancy (Figures 2B and 2C), respectively. Thus, this group represents individuals with BP levels similar to prehypertension. Moreover, based on a recent report on gestational age–specific reference ranges for BP in pregnancy,[33] the normal BP ranges should be between the low-J-shaped group and the moderate-U-shaped group. Consequently, the moderate-U-shaped group represents participants with BP levels between normal and prehypertension levels. Thus, our normotensive cohort-based, 3-trajectory group model is generally in agreement with a recent longitudinal study that modeled BP development in a cohort from childhood to early midlife into 4 trajectories (hypertensive, prehypertensive, high-normal, and normal).[32] The gestational BP trajectory groups for SBP, MAP, and mid-BP are shown in Figures S1 to S3 in the online-only Data Supplement.

We next examined which of the BP index-derived 3-trajectory models could best predict the occurrence of MetS postpartum. As shown in Table 2 of the 309 participants with available follow-up data, the patients in the elevated-J-shaped group had greater odds of having MetS than individuals in the low-J-shaped DBP trajectory group (odds ratio [OR], 5.16; 95% confidence interval, 1.56–17.05; $P=0.007$). Adjusting for the confounders that significantly differed in Table 1 (pregnancy age, body mass index [both at baseline and during follow-up], free fatty acid level, and neonatal weight) slightly increased the OR (OR, 6.55; 95% confidence interval, 1.79–23.92; $P=0.004$). However, patients in the moderate-U-shaped DBP trajectory did not have a statistically increased OR for having MetS. To examine the associations between a single measurement of BP, the participants were reclassified by diastolic BP (≥80 or <80 mm Hg) and SBP (≥120 or <120 mm Hg) levels at term. Compared with the patients without an elevated DBP level, the OR for postpartum MetS in patients with DBP prehypertension at term was significantly increased and remained statistically significant after adjusting for confounders (OR, 2.94; 95% confidence interval, 1.19–7.25; $P=0.019$). Notably, there was no association between SBP-derived, MAP-derived, and mid-BP–derived trajectory memberships, or SBP prehypertension at term, and postpartum MetS (Tables S1–S3).

Table 1. Baseline, Antepartum, Delivery, and Postpartum Characteristics in Total, MetS and Non-MetS Participants

Variable	Total (n=309)	Non-MetS (n=274; 88.7%)	MetS (n=35; 11.3%)	*P* Value
Baseline (11^{+0} to 13^{+6} wk)				
Maternal age, at delivery, y	29.76±4.24	29.56±4.21	31.31±4.19	0.02
Multipara, n (%)	108 (35)	93 (34)	15 (43)	0.30
BMI, baseline, kg/m^2	21.40±2.92	21.14±2.81	23.46±2.99	<0.001
SBP, baseline, mm Hg	108.69±8.59	108.58±8.59	110.28±8.88	0.42
DBP, baseline, mm Hg	67.15±7.36	66.85±7.30	71.67±6.91	0.01
HOMA-IR	1.07±0.45	1.04±0.43	1.23±0.58	0.16
FPG, mmol/L	4.31±0.28	4.30±0.29	4.42±0.24	0.12
Plasma insulin, U/L	5.53±2.17	5.42±2.05	6.21±2.77	0.23
Total cholesterol, mmol/L	5.05±0.87	5.10±0.88	4.73±0.77	0.16
HDL-C, mmol/L	1.71±0.41	1.70±0.39	1.76±0.49	0.66
LDL-C, mmol/L	2.44±0.56	2.48±0.58	2.22±0.36	0.13
Triglycerides, mmol/L	1.50±0.62	1.53±0.60	1.31±0.75	0.25
Free fatty acids, μg/L	543.64±239.86	532.82±239.03	607.67±245.79	0.32
Antepartum				
BMI, at term, kg/m^2	26.40±3.29	26.16±3.18	28.34±3.49	<0.001
SBP, at term, mm Hg	114.53±9.75	114.34±9.66	116.00±10.52	0.34
DBP, at term, mm Hg	70.28±7.94	70.04±7.66	72.20±9.73	0.13
HOMA-IR	1.92±1.27	1.88±1.26	2.24±1.31	0.11
FPG, mmol/L	4.42±0.63	4.38±0.60	4.75±0.76	0.001
Plasma insulin, U/L	9.46±5.03	9.34±4.98	10.37±5.40	0.26
Total cholesterol, mmol/L	5.58±1.12	5.65±1.12	5.05±0.90	0.003
HDL-C, mmol/L	1.45±0.35	1.49±0.35	1.19±0.30	<0.001
LDL-C, mmol/L	2.71±0.86	2.78±0.86	2.14±0.62	<0.001
Triglycerides, mmol/L	3.01±1.42	2.90±1.31	3.89±1.87	<0.001
Free fatty acids, μg/L	583.96±221.47	573.75±218.53	655.12±232.08	0.048
Delivery				
Gestational age at delivery, wk	38.95±1.31	38.98±1.30	38.71±1.41	0.26
Cesarean section, n (%)	173 (56)	152 (55)	21 (60)	0.61
Neonatal weight, g	3214±475	3182±444	3466±619	0.001
Postpartum follow-up				
Maternal age, y	31.19±4.70	30.97±4.73	32.94±4.05	0.02
Follow-up time, y	1.60±0.96	1.57±0.95	1.82±1.05	0.15
BMI, follow-up, kg/m^2	22.00±3.18	21.89±3.07	22.86±3.86	0.09
SBP, follow-up, mm Hg	107.09±11.44	105.64±10.34	118.43±13.37	<0.001
DBP, follow-up, mm Hg	69.91±8.56	68.77±7.76	78.83±9.40	<0.001
HOMA-IR	1.82±1.09	1.62±0.75	3.38±1.88	<0.001
FPG, mmol/L	5.09±0.57	4.99±0.42	5.89±0.88	<0.001
Plasma insulin, U/L	7.87±4.01	7.24±3.13	12.81±6.20	<0.001
Total cholesterol, mmol/L	4.91±1.20	4.90±1.22	5.20±0.48	0.52
HDL-C, mmol/L	1.24±0.25	1.27±0.25	1.06±0.15	<0.001
LDL-C, mmol/L	2.59±0.72	2.56±0.73	2.79±0.55	0.07

(*Continued*)

Table 1. Continued

Variable	Total (n=309)	Non-MetS (n=274; 88.7%)	MetS (n=35; 11.3%)	*P* Value
Triglycerides, mmol/L	1.04±0.59	0.92±0.40	2.03±0.84	<0.001
Waist circumference, cm	77.75±8.58	77.38±8.58	84.64±5.18	0.03
Waist circumference ≥80 cm (%)	73 (24)	50 (18)	23 (66)	<0.001
BP≥135/85 mm Hg (%)	19 (6)	7 (3)	12 (34)	<0.001
Triglycerides ≥1.7, mmol/L (%)	30 (10)	8 (3)	22 (63)	<0.001
HDL<1.3, mmol/L (%)	193 (62)	159 (58)	34 (97)	<0.001
FPG≥5.6, mmol/L (%)	34 (11)	14 (5)	20 (57)	<0.001

BMI indicates body mass index; BP, blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; MetS, metabolic syndrome; and SBP, systolic blood pressure.

Because the elevated-J-shaped DBP trajectory and DBP prehypertension at term were both associated with postpartum MetS, we sought to examine the associations between these 2 DBP categories and individual cardiometabolic risk factors during follow-up. Binary logistic regression analyses (Table S4) revealed that the elevated-J-shaped DBP trajectory was more likely to be associated with FPG and triglycerides levels, whereas an elevated DBP at term was more likely to be associated with increased waist circumference, elevated BP level, and reduced HDL-C level. In addition, when we combined the low-J-shaped and the moderated-U-shaped groups into 1 group and used the κ statistic to test the agreement between the elevated-J-shaped DBP trajectory and the elevated DBP at term, the level of agreement was considered fair, with κ=0.22 (criteria for κ value: poor if κ≤0.20; fair if κ=0.21–0.40; moderate if κ=0.41–0.60; substantial if κ=0.61–0.80; and very good if κ>0.80).[34] These results suggested that although the elevated-J-shaped DBP trajectory and DBP prehypertension at term both predicted postpartum MetS, the individuals in these 2 groups were heterogeneous.

To construct a prediction model for postpartum MetS, the receiver operator characteristic curve analyses showed that among the MetS definition–related components obtained at term (waist circumference is not applicable at this time), only FPG, triglycerides, HDL-C, and DBP trajectories had an AUC with statistical significance (Table S5). Because HDL-C and triglycerides were inversely correlated (Pearson r=–0.309; P<0.001), we thus built 2 models (FPG+DBP trajectories+HDL-C and FPG+DBP trajectories+triglycerides). Although these 2 models had similar discrimination capacities (c-statistic, 0.755 versus 0.764, for HDL-C and triglycerides models, respectively), the model incorporating HDL-C had poor calibration (Hosmer–Lemeshow test χ^2, 10.55; P=0.005; Table S6 and Figure S4). Consequently, the model incorporating FPG, DBP trajectories, and triglycerides provides the optimal prediction of postpartum MetS, with clinically acceptable discrimination (c-statistic, 0.764; 95% confidence interval, 0.674–0.855; P<0.001) and calibration (Hosmer–Lemeshow test χ^2, 1.85; P=0.764; Table 3; Figure 3) capacities.

Finally, we examined the changes in the MetS definition–related components during follow-up. As shown in Figure 4, compared with the MetS-related components at term, HDL-C underwent a decreasing trend with no significant difference between MetS and non-MetS participants. Despite a similar decreasing trend in triglycerides level, the reduction in MetS participants was smaller in magnitude than their non-MetS peers. The level of FPG was significantly increased during follow-up, with more obvious elevation in MetS participants. Notably, the relative changes in HOMA-IR, DBP, and SBP showed opposing trends, with increasing trends in MetS participants and decreasing trends in non-MetS participants. Multivariate linear regression analyses revealed that the levels

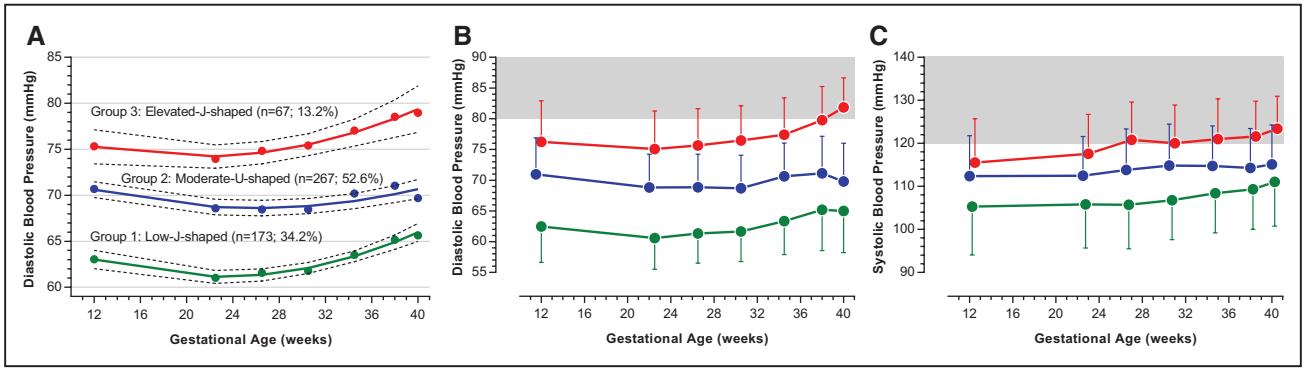

Figure 2. Diastolic blood pressure trajectories and corresponding blood pressure levels during pregnancy. **A**, Diastolic blood pressure trajectory groups identified by latent class growth modeling. **B** and **C**, The corresponding diastolic and systolic blood pressure levels to the 3 trajectory groups in **A**. The dashed lines in **A** indicate 95% confidence intervals. The data in **B** and **C** are shown as the means with SDs. The gray areas in **B** and **C** indicate the ranges of prehypertension.

Table 2. Univariate and Adjusted Multivariate Logistic Regression Analyses for 2 BP Categories (DBP Trajectory Groups and BP at Term) and Postpartum Metabolic Syndrome

BP Category	No. of Participants (%)	Odds Ratio (95% CI)			
		Univariate	*P* Value	Multivariate	*P* Value
DBP trajectory group					
Low-J-shaped	68 (22.0)	1 (Reference)		1 (Reference)	
Moderate-U-shaped	210 (68.0)	1.40 (0.51–3.87)	0.516	1.25 (0.43–3.62)	0.685
Elevated-J-shaped	31 (10.0)	5.16 (1.56–17.05)	0.007	6.55 (1.79–23.92)	0.004
Elevated DBP at term (≥80 mm Hg)					
No	274 (88.7)	1 (Reference)		1 (Reference)	
Yes	35 (11.3)	3.38 (1.48–7.74)	0.004	2.94 (1.19–7.25)	0.019
Elevated SBP at term (≥120 mm Hg)					
No	274 (88.7)	1 (Reference)			
Yes	35 (11.3)	1.23 (0.591–2.55)	0.581		

BP indicates blood pressure; CI, confidence interval; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

of HOMA-IR, FPG, and triglycerides were independently associated with SBP (Table S6) and DBP (Table S7) during follow-up.

Discussion

Despite accumulating evidence demonstrating the association between HDP and future CVD, the association between antepartum prehypertension and postpartum cardiovascular risk has not been investigated. Using latent class growth modeling from multiple BP measurements obtained throughout the course of pregnancy, we identified 3 distinctive DBP trajectory groups during normotensive pregnancies associated with postpartum MetS. The elevated-J-shaped trajectory group (13.2% of total cohort), which is characterized by the highest DBP and SBP levels throughout pregnancy and a steep rise during the third trimester, with mean DBP and SBP levels within the range of prehypertension at term, had an ≈5-fold increase in developing postpartum MetS compared with the low-J-shaped group. Moreover, incorporating the DBP trajectory, but not the DBP prehypertension defined by a single measurement at term, with glucose and triglycerides provided a prediction model with clinically acceptable discrimination (AUC of 0.7–0.8[35]) and good calibration. Thus, our data suggest that prehypertension identified by DBP trajectories throughout pregnancy is an independent risk factor for predicting postpartum MetS in normotensive pregnant women

Interestingly, we did not observe statistical associations between the other BP-derived trajectory groups (SBP, MAP, and mid-BP) and postpartum MetS, presumably because of the more dramatic impact of pregnancy on DBP that is induced by alterations in systemic vascular resistance.[36] In fact, DBP has been shown to play a larger role in coronary heart disease risk among young to middle-aged adults.[37] Notably, although both DBP trajectories and a single DBP reading at term could identify a subset of women with higher risk of future MetS, the participants classified by these 2 approaches were heterogeneous. Moreover, a single DBP measurement did not play a statistically important role in the prediction model of postpartum MetS. In recent years, the emerging application of multiple BP measurement-derived trajectories across the lifespan has provided insights for identifying novel means of preventing future cardiovascular risk.[30,32,38] Therefore, considering the dynamic nature of BP during pregnancy and the impact of seasonality on pregnancy BP levels,[39] BP trajectories that are an entire pregnancy course-dependent systemic approach have potential advantages over the fragmented, single BP measurement in terms of accuracy and reproducibility. Because all pregnant women should have at least 4 antenatal care assessments according to the new World Health Organization antenatal care model,[40] full utilization of these serial BP data would thus provide additional information for future risk stratification.

There is an expanding burden of cardiometabolic risk in women, and it is a major contributor to CVD both in China

Table 3. Multiple Logistic Regression Analyses for the Construction of Prediction Model for Postpartum Metabolic Syndrome by Bootstrap Method (Incorporating Triglycerides)

Variable	Coefficient (β)			Odds Ratio			*P* Value
	Observed	Bootstrap SE	95% CI	Observed	Bootstrap SE	95% CI	
FPG (>4.99 mmol/L or not)	1.67	0.42	0.85 to 2.49	5.29	2.22	2.33 to 12.02	<0.001
Triglycerides (>3.14 mmol/L or not)	1.47	0.45	0.58 to 2.35	4.34	1.96	1.79 to 10.53	0.001
Elevated-J-shaped trajectory (yes/no)	1.25	0.51	0.24 to 2.26	3.50	1.81	1.27 to 9.62	0.015
Constant	-3.42	0.44	−4.28 to −2.56	0.03	0.01	0.01 to 0.08	<0.001

CI indicates confidence interval; and FPG, fasting plasma glucose.

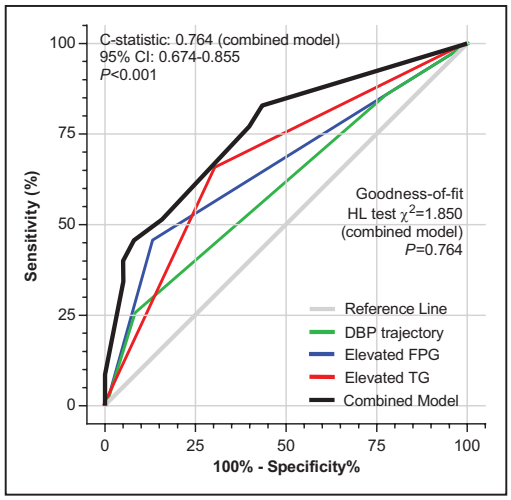

Figure 3. Receiver operating characteristic (ROC) curve for multiple logistic regression analyses. The multiple logistic regression equation used to construct the ROC curve (black line) is as follows: logit(y)=−3.42+(1.25×diastolic BP [DBP]_trajectory) + (1.47×triglycerides [TG])+(1.67×fasting plasma glucose [FPG]). The optimal cutoff values for each variable are shown in Table 3. CI indicates confidence interval; and HL, Hosmer–Lemeshow.

and in worldwide.[41,42] Approximately 80% of women in developed countries and 90% in developing countries will have at least 1 pregnancy in their life time.[43] Pregnancy is characterized by a cascade of physiological changes that poses a substantial burden on BP regulation, as well as on glucose and lipid metabolism. Thus, pregnancy perfectly unmasks defects in BP regulation when the body is dealing with hemodynamic alterations. In addition, the pregnancy-induced resetting of glucose and lipid homeostasis, as manifested by decreased insulin sensitivity and increased circulating triglycerides, mimic the pathological alterations observed in MetS.[44] Recent data showed that in addition to gestational diabetes mellitus, even mild forms of dysglycemia during pregnancy represent a maternal phenotype of increased subsequent cardiometabolic risk.[45] Our data revealed that the MetS participants underwent a progressive worsening of glucose metabolism from enrollment at gestational age of 11^{+0} to 13^{+6} weeks, to at term, and

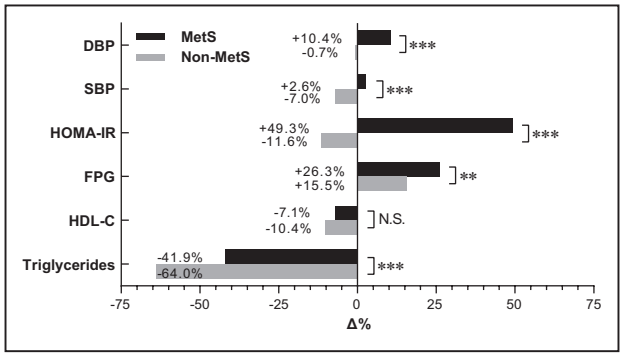

Figure 4. The changes in the metabolic syndrome (MetS) definition–related components during follow-up vs those at term. The Δ% is defined as follows: $(value_{follow\text{-}up}-value_{at\ term})/value_{at\ term}\times100\%$. DBP indicates diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment of insulin resistance; N.S., not significant; and SBP, systolic blood pressure. $^{**}P<0.01$, $^{***}P<0.001$.

to ≈1.6 years postpartum. This finding is consistent with a recent report that β-cell function declines within the first year postpartum.[46] Moreover, our finding that HOMA-IR independently predicts postpartum BP level further supports insulin resistance as the underlying pathophysiological mechanism contributing to elevated BP level.

Our study has limitations that need to be mentioned. First, the follow-up rate in our study was ≈60%, which is generally regarded as a low rate for cohort studies. However, our cohort was drawn from a normotensive and uncomplicated population, and patients who are completely or nearly asymptomatic are less likely to be self-motivated for long-term follow-up. The low follow-up rate is a common issue for postpartum women; even among preeclamptic women with continuous medical coverage, only 57% of subjects attended a primary care visit within 1 year after delivery.[47] By applying strict enrollment criteria to exclude a potentially mobile population of young families, our study had a higher follow-up rate than previously published studies on pregnant women.[48,49] Second, because our study is based on the Chinese population and because of the ethnic variation in the individual components of MetS,[50] the generalizability of our results to other ethnic populations warrants future analysis. Third, we did not collect data on self-reported smoking in our study, which is a well-known confounder for BP changes during pregnancy.[51] Because the smoking rate among Chinese men is ≈70%,[52] future work is warranted to examine the potential impact of passive smoking exposure using information provided by serum nicotine measurements. Fourth, as a common limitation in pregnant women, the lack of preconception information may contribute to the uncertainty of whether the elevated BP level in a subset of pregnant women is because of failed stress response to pregnancy or because of preconception disorders. However, we performed a thorough screening at baseline (11^{+0}–13^{+6} weeks) including glucose and lipid profiles, which could minimize the impact of this limitation. Fifth, external validation in an independent cohort is necessary, and the current DBP trajectories and related prediction model cannot be widely implemented.

Our study has the following strengths. We used a new statistical approach, latent class growth modeling, also known as group-based trajectory modeling, which was recently developed to identify clusters of individuals after a similar progression of a specific measurement over age or time.[26] This method has been utilized and reported in recent longitudinal studies involving multiple BP measurements.[30,32,53] To our knowledge, our report is the first to use this method to delineate BP patterns during pregnancy. Because BP measurement is a part of a routine prenatal check-up, our findings provide evidence demonstrating a novel method to cost-effectively estimate future cardiovascular risk among women. Moreover, future work is warranted to examine the potential role of a more intensive BP management strategy during pregnancy, which has been recently demonstrated to clinically benefit a nonpregnant population in the Systolic Blood Pressure Intervention Trial (SPRINT) study.[54]

Early identification of metabolic risk factors and the implementation of lifestyle modifications may help delay the onset of CVD that may present 20 to 30 years after delivery and consequently improve women's health status and quality of

life. Although a BP ≥140/90 mm Hg is a well-known risk factor for cardiovascular risk during pregnancy and postpartum, our findings suggest that individuals with DBP prehypertension identified by multiple BP measurement-based trajectory modeling throughout pregnancy are at an increased risk of postpartum MetS. Our study highlights the potential role of antepartum prehypertension in postpartum cardiovascular risk stratification and fortifies the emerging concept that the individualized mapping of multiple BP measurements over time may provide additional information on an individual's cardiovascular risk status.

Perspectives

The prognostic role of prehypertension (120–139/80–89 mm Hg) during pregnancy for postpartum cardiovascular risk is unclear. In this study, we prospectively evaluated the relationship between antepartum BP trajectories and the occurrence of postpartum MetS and demonstrated that the DBP trajectory within the range of prehypertension is an independent risk factor predicting postpartum MetS. This finding highlights the multiple BP measurement-dependent trajectories as a cost-effective strategy to identify subgroups of young women for whom early cardiovascular risk factor surveillance may be warranted.

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Disclosures

None.

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Novelty and Significance

What Is New?

- The exposure to prehypertension during pregnancy, as identified by diastolic blood pressure (BP) trajectories using multiple diastolic BP measurements, is an independent risk factor for developing postpartum metabolic syndrome.
- The incorporation of diastolic BP trajectories with the levels of glucose and triglycerides at term provides a novel prediction model for postpartum metabolic syndrome.

What Is Relevant?

- Our data highlight the need for the reevaluation of the pregnancy-specific BP range using multiple BP measurements for postpartum cardiovascular risk stratification.

Summary

Normotensive pregnant women with prehypertension identified by multiple diastolic BP measurement-dependent trajectories throughout pregnancy have an increased risk of developing postpartum metabolic syndrome.

Prehypertension During Normotensive Pregnancy and Postpartum Clustering of Cardiometabolic Risk Factors: A Prospective Cohort Study

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Table S1. Univariate and multivariate logistic regression analyses for BP trajectory groups and postpartum MetS

BP trajectory group	No.(%) of participants	OR (95% CI)			
		Univariate	*P*	multivariate	*P*
SBP trajectory group					
Low-J-shaped	15 (5)	1 [Reference]			
Moderate-Stable	230 (74)	1.71 (0.22-13.54)	0.61		
Elevated-Stable	64 (21)	2.29 (0.27-19.62)	0.45		
MAP trajectory group					
Low-J-shaped	38 (12)	1 [Reference]		1 [Reference]	
Moderate-U-shaped	231 (75)	4.69 (0.61-35.65)	0.14	3.93 (0.50-30.80)	0.19
Elevated-Stable	40 (13)	9.25 (1.10-78.00)	0.04	7.26 (0.83-63.85)	0.07
Mid-BP trajectory group					
Low-J-shaped	21 (7)	1 [Reference]			
Moderate-U-shaped	227 (74)	2.48 (0.32-19.25)	0.39		
Elevated-Stable	61 (20)	3.46 (0.41-29.11)	0.25		

BP =blood pressure; OR=Odds Ratio; CI=confidence of interval; MetS=metabolic syndrome; SBP=systolic blood pressure; MAP= mean arterial pressure；

Table S2. Baseline, antepartum, delivery and postpartum characteristics in three shaped DBP trajectories during pregnancy and DBP prehypertension at term participants

Variable	DBP Trajectories			*P*	DBP prehypertension at term (≥80mmHg)		*P*
	Low-J-Shaped (n=68; 22%)	Moderate-U-Shaped (n=210; 68%)	Elevated-J-Shaped (n=31; 10%)		No (n=270; 87%)	Yes (n=39; 13%)	
Baseline Information							
Maternal age delivery (yr)	30.13±4.48	29.71±4.12	29.26±4.57	0.61	29.70±4.28	30.18±4.00	0.51
Multipara, No. (%)	27(40)	72(34)	9(29)	0.55	91(34)	17(44)	0.23
BMI, baseline(kg/m^2)	20.89±2.55	21.52±3.07	21.71±2.49	0.25	21.32±2.76	21.98±3.83	0.18
SBP, baseline (mmHg)	100.38±9.22	109.59±7.97	115.96±8.91	<0.001	110.24±9.17	110.66±8.37	0.72
DBP, baseline (mmHg)	66.46±7.28	68.64±6.86	70.69±6.74	0.07	69.15±6.69	68.57±7.27	0.52
HOMA-IR	1.05±0.43	1.04±0.47	1.13±0.43	0.70	1.04±0.43	1.23±0.58	0.16
FPG (mmol/L)	4.28±0.11	4.33±0.31	4.26±0.22	0.61	4.29±0.29	4.42±0.24	0.12
Plasma insulin (U/L)	5.54±2.18	5.37±2.22	5.94±2.07	0.56	5.42±2.05	6.21±2.77	0.23
TCH (mmol/L)	4.60±0.48	5.13±0.89	4.93±0.87	0.33	5.10±0.88	4.73±0.77	0.16
HDL-C (mmol/L)	1.74±0.21	1.76±0.41	1.58±0.40	0.20	1.70±0.39	1.76±0.49	0.66
LDL-C (mmol/L)	2.06±0.18	2.50±0.56	2.38±0.57	0.20	2.48±0.58	2.22±0.36	0.13
TG(mmol/L)	1.37±0.29	1.50±0.64	1.54±0.65	0.86	1.53±0.60	1.31±0.75	0.25
Apolipoprotein A1 (g/L)	2.99±0.81	2.95±0.99	2.56±1.30	0.31	2.86±1.07	2.77±1.17	0.79
Apolipoprotein B (g/L)	0.76±0.07	0.92±0.19	1.02±0.45	0.14	0.96±0.30	0.82±0.13	0.11
Free fatty acids (μg/L)	493.60±233.19	566.19±259.55	503.33±192.33	0.51	532.82±239.03	607.67±245.08	0.32
Antepartum Information							
BMI, at term(kg/m^2)	26.31±3.27	26.46±3.44	26.24±2.20	0.91	26.32±3.12	27.00±4.28	0.22
SBP, at term(mmHg)	111.65±9.48	115.13±9.65	116.77±10.04	0.02	113.28±9.48	123.18±6.85	<0.001
DBP, at term(mmHg)	68.76±9.26	70.13±7.10	74.68±8.84	0.002	68.34±6.39	83.72±3.02	<0.001
HOMA-IR	1.97±1.82	1.85±1.00	2.31±1.41	0.16	1.87±1.22	2.24±1.56	0.09

FPG (mmol/L)	4.37±0.60	4.40±0.62	4.69±0.71	0.04	4.39±0.58	4.65±0.87	0.02
Plasma insulin (U/L)	9.69±6.85	9.22±4.23	10.55±5.37	0.36	9.35±4.97	10.19±5.44	0.34

Table S2 Continued

Variable	DBP Trajectories				DBP prehypertension at term (≥80mmHg)		
	Low-J-Shaped (n=68; 22%)	Moderate-U-Shaped (n=210; 68%)	Elevated-J-Shaped (n=31; 10%)	*P*	No (n=270; 87%)	Yes (n=39; 13%)	*P*
TCH (mmol/L)	5.69±1.33	5.54±1.06	5.63±0.98	0.63	5.62±1.12	5.32±1.03	0.11
HDL-C (mmol/L)	1.46±0.31	1.45±0.36	1.42±0.39	0.81	1.46±0.35	1.39±0.36	0.26
LDL-C (mmol/L)	2.76±0.99	2.69±0.84	2.69±0.75	0.83	2.73±0.88	2.51±0.73	0.14
TG(mmol/L)	3.10±1.54	2.95±1.33	3.22±1.69	0.50	3.02±1.47	2.95±1.03	0.77
Apolipoprotein A1 (g/L)	1.78±0.41	1.80±0.43	1.83±0.40	0.94	1.81±0.42	1.74±0.44	0.50
Apolipoprotein B (g/L)	1.24±0.28	1.25±0.28	1.03±0.20	0.03	1.23±0.28	1.26±0.28	0.67
Free fatty acids (μg/L)	582.31±254.54	582.67±208.41	596.50±243.76	0.96	583.36±212.63	587.91±275.81	0.91
Delivery Information							
Gestational age at delivery (wks)	38.94±1.3	38.96±1.27	38.90±1.62	0.98	38.97±1.32	38.82±1.23	0.52
Neonatal weight (g)	3207±500	3250±398	3181±469	0.75	3203±466	3289±534	0.29
Cesarean section, No. (%)	33(49)	127(60)	13(42)	0.06	154(57)	19(49)	0.33
Postpartum Follow-up Information							
Maternal age (yr)	31.64±4.82	31.26±4.70	30.19±4.41	0.44	31.03±4.77	32.36±3.98	0.10
Follow-up time (yr)	1.56±0.93	1.60±0.97	1.68±1.00	0.85	1.58±0.96	1.72±0.96	0.40
BMI, follow-up(kg/m^2)	22.11±3.34	22.06±3.23	21.29±2.35	0.42	21.88±2.96	22.77±4.39	0.11
SBP, follow-up(mmHg)	103.44±11.05	107.30±10.98	113.68±12.50	<0.001	106.60±10.62	110.51±15.76	0.046
DBP, follow-up(mmHg)	67.50±8.06	69.94±8.36	74.97±8.97	<0.001	69.33±7.91	73.90±11.48	0.002
HOMA-IR	1.64±0.71	1.84±1.19	2.07±1.03	0.18	1.75±1.03	2.29±1.38	0.004
FPG (mmol/L)	5.04±0.54	5.09±0.54	5.26±0.72	0.18	5.06±0.52	5.31±0.80	0.01
Plasma insulin (U/L)	7.27±2.86	7.94±4.33	8.72±3.83	0.23	7.64±3.85	9.43±4.75	0.01

TCH(mmol/L)	4.70±0.97	4.98±1.28	4.98±1.16	0.50	4.95±1.20	4.63±1.18	0.30
HDL-C (mmol/L)	1.24±0.25	1.25±0.25	1.21±0.24	0.84	1.26±0.25	1.16±0.23	0.02
LDL-C (mmol/L)	2.54±0.66	2.59±0.75	2.66±0.63	0.75	2.60±0.72	2.53±0.68	0.58

Table S2 Continued

Variable	DBP Trajectories				DBP prehypertension at term (≥80mmHg)		
	Low-J-Shaped (n=68; 22%)	Moderate-U-Shaped (n=210; 68%)	Elevated-J-Shaped (n=31; 10%)	*P*	No (n=270; 87%)	Yes (n=39; 13%)	*P*
TG (mmol/L)	1.03±0.56	1.02±0.55	1.25±0.83	0.12	1.02±0.57	1.20±0.67	0.06
Apolipoprotein A1 (g/L)	1.61±0.41	1.68±0.40	1.73±0.46	0.63	1.68±0.40	1.62±0.45	0.57
Apolipoprotein B (g/L)	1.02±0.37	1.03±0.34	1.04±0.23	0.97	1.03±0.34	1.06±037	0.72
Waist circumstance (cm)	77.76±8.13	77.40±8.50	80.15±10.40	0.56	77.42±8.79	80.06±6.65	0.24
Waist currcustance≥80cm (%)	18(26)	45(21)	10(32)	0.34	58(21)	15(38)	0.02
BP≥135/85mmHg (%)	3(4)	11(5)	5(16)	0.05	10(4)	9(23)	<0.001
TG ≥1.7 (mmol/L) (%)	6(9)	17(8)	7(23)	0.04	24(9)	6(15)	0.20
HDL-C<1.3(mmol/L) (%)	45(66)	127(60)	21(68)	0.57	161(60)	32(82)	0.007
FPG≥5.6 (mmol/L) (%)	4(6)	23(11)	7(23)	0.048	27(10)	7(18)	0.14

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; HOMA-IR= homeostatic model assessment of insulin resistance; TCH=total cholesterol；FPG=fasting plasma glucose; HDL-C=high density lipoprotein cholesterol; LDL-C=low density

Table S3. Baseline, antepartum, delivery and postpartum characteristics in SBP, MAP, Mid-BP trajectories during pregnancy

Variable	SBP trajectories				MAP trajectories				Mid-BP trajectories			
	Low-J-shaped	Moderate-	Elevated-	*P*	Low-J-shaped	Moderate-U-	Elevated-	*P*	Low-J-shaped	Moderate-U-	Elevated-	*P*
Baseline Information												
Maternal age, delivery	29.13±4.26	29.93±4.33	29.31±3.88	0.50	30.00±4.90	29.65±4.06	30.20±4.65	0.70	29.14±5.03	29.87±4.12	29.57±4.43	0.70
Multipara, No (%)	6(40)	86(37)	16(25)	0.17	38(39)	231(34)	40(35)	0.82	8(38)	81(36)	19(31)	0.77
BMI, baseline (kg/m^2)	20.44±2.74	21.38±3.05	21.70±2.42	0.32	20.60±2.60	21.40±2.99	22.14±2.61	0.07	20.25±2.05	21.38±3.08	21.88±2.43	0.08
SBP, baseline (mmHg)	107.85±9.71	111.14±8.37	110.50±9.78	0.05	104.25±9.47	110.45±7.90	115.82±10.16	<0.001	101.94±9.18	109.75±7.83	115.80±9.68	<0.001
DBP, baseline (mmHg)	64.40±8.10	69.69±5.89	73.23±6.17	<0.001	62.38±8.02	69.25±6.01	73.32±6.43	<0.001	63.35±8.54	68.47±6.44	72.68±6.33	<0.001
HOMA-IR	1.03±0.53	1.06±0.46	1.12±0.40	0.86	1.01±0.50	1.06±0.46	1.09±0.42	0.94	1.07±0.60	1.07±0.48	1.06±0.39	0.99
FPG (mmol/L)	4.28±0.17	4.32±0.31	4.28±0.19	0.88	4.28±0.12	4.31±0.30	4.30±0.25	0.94	4.28±0.15	4.33±0.31	4.27±0.23	0.70
Plasma insulin (U/L)	5.36±2.68	5.48±2.17	5.86±1.97	0.82	5.33±2.59	5.50±2.21	5.68±2.03	0.93	5.63±3.08	5.53±2.29	5.52±1.91	1.00
TCH (mmol/L)	4.51±0.0.71	5.09±0.88	5.13±0.88	0.19	4.44±0.36	5.15±0.87	4.84±0.90	0.14	4.36±0.39	5.10±0.88	5.00±0.88	0.33
HDL-C (mmol/L)	1.64±0.22	1.72±0.42	1.69±0.46	0.87	1.69±0.13	1.75±0.41	1.58±0.41	0.29	1.63±0.01	1.74±0.41	1.66±0.43	0.64
LDL-C (mmol/L)	2.12±0.44	2.47±0.56	2.46±0.60	0.23	2.00±0.17	2.51±0.55	2.29±0.57	0.08	1.98±0.20	2.48±0.56	2.40±0.57	0.29
TG (mmol/L)	1.16±0.28	1.51±0.61	1.66±0.77	0.20	1.18±0.23	1.51±0.62	1.52±0.69	0.59	1.23±0.25	1.53±0.64	1.46±0.62	0.66
Apolipoprotein A1(g/L)	2.60±0.64	2.89±1.11	2.76±1.19	0.73	2.74±0.67	2.93±1.11	2.61±1.06	0.50	2.76±0.82	2.91±0.93	2.74±1.37	0.80
Apolipoprotein B (g/L)	0.77±0.16	0.92±0.18	1.12±0.59	0.02	0.74±0.07	0.93±0.18	1.01±0.50	0.21	0.73±0.09	0.92±0.19	1.00±0.42	0.22
Free fatty acids (μg/L)	517.43±214.20	557.89±239.22	482.92±265.43	0.59	418.33±295.79	562.82±244.78	504.90±218.67	0.43	418.33±295.79	593.20±253.55	469.45±188.64	0.05
Antepartum Information												
BMI, at term (kg/m^2)	25.23±3.01	26.33±3.47	26.95±2.52	0.15	25.99±3.18	26.37±3.46	26.99±2.17	0.39	26.14±	26.27±3.50	26.98±2.28	0.31
SBP, at term (mmHg)	108.27±9.15	114.48±9.40	116.17±10.61	0.02	110.82±9.86	114.57±9.42	117.83±10.53	0.006	110.00±9.89	114.24±9.26	117.16±10.89	0.01
DBP, at term (mmHg)	67.80±11.94	70.21±7.47	71.13±8.45	0.33	66.47±9.00	70.30±7.32	73.83±8.71	<0.001	67.24±9.67	70.05±7.53	72.20±8.46	0.03
HOMA-IR	1.84±1.30	1.88±1.19	2.07±1.53	0.56	1.68±0.94	1.91±1.31	2.19±1.32	0.21	1.73±1.06	1.92±1.31	2.00±1.20	0.69
FPG (mmol/L)	4.32±0.49	4.42±0.63	4.46±0.67	0.73	4.32±0.53	4.39±0.62	4.71±0.70	0.008	4.41±0.58	4.39±0.62	4.54±0.68	0.28
Plasma insulin (U/L)	9.25±5.67	9.30±4.54	10.04±6.43	0.58	8.52±4.16	9.50±5.14	10.09±5.17	0.37	8.57±4.53	9.52±5.15	9.55±4.80	0.70
TCH (mmol/L)	5.67±0.72	5.55±1.14	5.68±1.10	0.68	5.46±1.09	5.60±1.12	5.62±1.15	0.78	5.81±0.95	5.55±1.13	5.61±1.13	0.59
HDL-C (mmol/L)	1.41±0.29	1.46±0.35	1.43±0.37	0.79	1.44±0.34	1.46±0.35	1.41±0.37	0.71	1.48±0.28	1.46±0.36	1.43±0.35	0.79
LDL-C (mmol/L)	2.67±0.74	2.69±0.86	2.79±0.89	0.71	2.64±0.73	2.72±0.87	2.72±0.96	0.88	2.77±0.79	2.70±0.86	2.72±0.91	0.92
TG (mmol/L)	3.52±2.11	2.98±1.38	3.01±1.37	0.36	3.08±1.60	2.98±1.36	3.09±1.58	0.86	3.39±1.99	2.98±1.36	2.98±1.40	0.45
Apolipoprotein A1(g/L)	1.81±0.41	1.84±0.45	1.66±0.31	0.10	1.80±0.35	1.81±0.45	1.70±0.28	0.65	1.86±0.36	1.83±0.45	1.65±0.28	0.14

Table S3 Continued

Variable	SBP trajectories				MAP trajectories				Mid-BP trajectories			
	Low-J-shaped	Moderate-	Elevated-	*P*	Low-J-shaped	Moderate-U-	Elevated-	*P*	Low-J-shaped	Moderate-U-	Elevated-	*P*
Apolipoprotein B (g/L)	1.13±0.24	1.25±0.28	1.20±0.28	0.40	1.18±0.22	1.26±0.29	1.07±0.23	0.044	1.19±0.23	1.25±0.29	1.19±0.29	0.58
Free fatty acids (μg/L)	518.54±337.38	590.40±207.54	575.81±29.77	0.51	555.34±259.04	591.06±212.78	569.79±236.98	0.65	550.18±320.87	594.95±211.49	551.51±220.89	0.38
Delivery Information												
Gestational age, delivery	39.13±1.00	38.95±1.30	38.89±1.42	0.81	39.00±1.19	38.93±1.32	39.00±1.36	0.92	38.81±1.44	38.97±1.28	38.90±1.39	0.82
Cesarean section, No (%)	7(47)	123(53)	43(67)	0.11	19(50)	131(57)	23(58)	0.73	10(48)	126(56)	37(61)	0.56
Neonatal weight (g)	3288±421	3200±485	3247±454	0.65	3203±444	3203±486	3288±441	0.57	3227±301	3195±496	3281±440	0.45
Postpartum Follow-up Information												
Maternal age (yr)	30.20±5.07	31.54±4.68	30.17±4.57	0.08	30.53±5.13	31.31±4.63	31.18±4.73	0.64	29.62±5.39	31.55±4.58	30.43±4.77	0.07
Follow-up time (yr)	1.60±1.00	1.57±0.97	1.71±0.91	0.58	1.42±0.99	1.63±0.96	1.61±0.94	0.47	1.65±0.91	1.58±0.98	1.66±0.90	0.85
BMI, follow-up(kg/m^2)	21.22±1.99	22.15±3.27	21.63±3.03	0.33	21.53±2.65	22.16±3.31	21.50±2.82	0.30	21.88±2.67	22.03±3.22	21.89±3.1	0.94
SBP, follow-up (mmHg)	100.67±12.72	107.16±10.95	108.36±12.53	0.06	101.47±11.07	107.30±10.07	111.20±12.60	0.001	100.29±10.37	106.83±10.80	110.41±13.02	0.002
DBP, follow-up (mmHg)	67.73±9.23	69.77±8.41	70.91±8.93	0.39	66.11±7.57	70.02±8.30	72.88±9.73	0.002	66.62±7.52	69.54±8.39	72.41±9.03	0.01
HOMA-IR	1.76±1.32	1.77±1.06	1.99±1.17	0.35	1.56±0.65	1.83±1.15	1.97±1.08	0.24	1.51±0.64	1.80±1.10	2.00±1.18	0.17
FPG (mmol/L)	4.95±0.34	5.05±0.52	5.28±0.72	0.01	4.94±0.30	5.07±0.53	5.39±0.83	0.001	4.98±0.25	5.05±0.53	5.29±0.72	0.01
Plasma insulin (U/L)	7.81±5.16	7.73±3.81	8.37±4.43	0.53	7.10±2.88	7.95±4.21	8.11±3.72	0.44	6.77±2.76	7.82±3.96	8.41±4.50	0.26
TCH (mmol/L)	4.73±0.73	4.84±1.25	5.18±1.11	0.36	4.59±0.83	4.93±1.26	5.22±1.10	0.33	4.69±0.82	4.84±1.24	5.31±1.16	0.15
HDL-C (mmol/L)	1.31±0.32	1.24±0.24	1.25±0.25	0.56	1.24±0.29	1.25±0.24	1.23±0.26	0.95	1.25±0.30	1.24±0.24	1.24±0.25	1.00
LDL-C (mmol/L)	2.55±0.64	2.57±0.68	2.67±0.85	0.59	2.46±0.64	2.58±0.70	2.73±0.83	0.25	2.59±0.58	2.55±0.70	2.72±0.80	0.24
TG (mmol/L)	0.95±0.37	1.04±0.58	1.07±0.66	0.79	0.89±0.33	1.06±0.59	1.09±0.74	0.22	0.91±0.34	1.06±0.59	1.02±0.64	0.52
Apolipoprotein A1 (g/L)	1.74±0.42	1.63±0.39	1.76±0.45	0.26	1.61±0.40	1.67±0.40	1.74±0.48	0.69	1.66±0.42	1.64±0.40	1.77±0.44	0.39
Apolipoprotein B (g/L)	1.16±0.59	0.99±0.31	1.12±0.33	0.09	1.02±0.46	1.03±0.32	1.09±0.32	0.80	1.08±0.48	1.00±0.29	1.16±0.39	0.06
Waist circumstance (cm)	74.33±7.94	77.46±7.83	79.65±10.63	0.22	77.00±7.40	77.44±7.73	81.04±14.37	0.31	77.25±7.86	77.21±7.74	80.02±11.47	0.33
Waist currcustance,	5(33)	49(21)	19(30)	0.25	9(24)	52(23)	12(30)	0.59	7(33)	48(21)	18(30)	0.22
BP≥135/85mmHg (%)	1(7)	14(6)	4(6)	1.00	1(3)	13(6)	5(13)	0.16	0(0)	13(6)	6(10)	0.38
TG ≥1.7 (mmol/L) (%)	1(7)	22(10)	7(11)	0.87	0(0)	25(11)	5(13)	0.09	0(0)	25(11)	5(8)	0.24
HDL-C＜1.3 (mmol/L)	9(60)	145(63)	39(61)	0.94	26(68)	142(61)	25(63)	0.72	14(67)	141(62)	38(62)	0.92
FPG≥5.6 (mmol/L) (%)	1(7)	20(9)	13(20)	0.03	0(0)	24(10)	10(25)	0.002	0(0)	22(10)	12(20)	0.02

BMI=body mass index; SBP=systolic blood pressure; DBP=diastolic blood pressure; HOMA-IR= homeostatic model assessment of insulin resistance; FPG=fasting plasma glucose; TCH=total cholesterol；HDL-C=high density lipoprotein cholesterol; LDL-C=low density lipoprotein cholesterol; TG=triglycerides

Table S4. The associations between diastolic blood pressure trajectory groups, diastolic blood pressure prehypertension at term and individual component of MetS

Variable	DBP trajectories (Odds Ratio [95% CI])					DBP prehypertension at term (≥80 mmHg) (Odds Ratio [95% CI])		
	low-J-shaped	moderate-U-shaped	*P*	elevated-J-shaped	*P*	No	Yes	*P*
Waist								
Univariate	1[Reference]	0.76(0.40-1.43)	0.39	1.32(0.52-3.34)	0.55	1[Reference]	2.28(1.13-4.64)	0.02
Multivariate	1[Reference]	0.97(0.45-2.09)	0.93	1.81(0.61-5.38)	0.29	1[Reference]	3.19(1.45-7.03)	0.004
FPG								
Univariate	1[Reference]	1.97(0.66-5.91)	0.23	4.67(1.25-17.38)	0.02	1[Reference]	1.97(0.79-4.89)	0.14
Multivariate	1[Reference]	1.64(0.52-5.16)	0.40	4.24(1.07-16.89)	0.04	1[Reference]	1.57(0.59-4.17)	0.37
HDL-C								
Univariate	1[Reference]	0.78(0.44-1.39)	0.40	1.07(0.43-2.65)	0.88	1[Reference]	3.10(1.32-7.26)	0.009
Multivariate	1[Reference]	0.57(0.28-1.13)	0.11	1.19(0.38-3.68)	0.77	1[Reference]	3.10(1.13-8.54)	0.03
Triglycerides								
Univariate	1[Reference]	0.91(0.34-2.41)	0.85	3.01(0.92-9.89)	0.07	1[Reference]	1.86(0.71-4.89)	0.21
Multivariate	1[Reference]	1.05(0.32-3.44)	0.94	5.86(1.42-24.16)	0.01	1[Reference]	1.77(0.62-5.04)	0.29
Blood pressure								
Univariate	1[Reference]	1.20(0.32-4.43)	0.79	4.17(0.93-18.71)	0.06	1[Reference]	7.80(2.94-20.71)	<0.005
Multivariate	1[Reference]	0.81(0.20-3.30)	0.77	3.65(0.68-19.47)	0.13	1[Reference]	6.72(2.23-20.25)	0.001

DBP=diastolic blood pressure; CI=confidence of interval; MetS=metabolic syndrome; FPG=fasting plasma glucose; HDL-C=high density lipoprotein cholesterol.

Table S5. Receiver operator characteristic curve analyses of MetS-definition related components at term for the prediction of postpartum MetS

Variable	AUC (95% CI)	*P*	Youden Index	Cut-off value	Sensitivity	Specificity
FPG (mmol/L)	0.637 (0.581-0.691)	0.015	0.333	>4.99 mmol/L	45.7%	87.6%
HDL-C (mmol/L)	0.682 (0.627-0.733)	<0.001	0.281	=<1.4 mmol/L	68.6%	59.5%
Triglycerides (mmol/L)	0.695 (0.640-0.746)	<0.001	0.351	>3.14 mmol/L	65.75	69.3%
DBP trajectories	0.608 (0.551-0.663)	0.044	0.177	>2	25.7%	92.0%
DBP Prehypertension (Yes/No)	0.590 (0.533-0.645)	0.104	0.180	Yes	28.6%	89.4%
DBP_continuous (mmHg)	0.550 (0.492-0.606)	0.393	0.202	>80 mmHg	28.6%	91.6%
SBP trajectories	0.536 (0.478-0.592)	0.493	0.056	>2	25.7%	79.9%
SBP Prehypertension (Yes/No)	0.523 (0.466-0.580)	0.657	0.047	Yes	37.1%	67.5%
SBP_continuous (mmHg)	0.540 (0.483-0.597)	0.464	0.122	>125 mmHg	25.7%	86.5%

MetS=metabolic syndrome; AUC=area under curve; CI=confidence interval; HDL-C=high density lipoprotein cholesterol; FPG=fasting plasma glucose; DBP=diastolic blood pressure; SBP=systolic blood pressure. Codes for DBP trajectories: 1=low-J-shaped trajectory; 2=moderate-U-shaped trajectory; 3=elevated-J-shaped trajectory (See Figure 2); Codes for SBP trajectories: 1=low-J-shaped trajectory; 2=moderate-stable trajectory; 3=elevated-stable trajectory (see Supplemental Figure S1).

Table S6. Multiple logistic regression analyses for the construction of prediction model of postpartum MetS by bootstrap method (incorporating HDL-C)

Variable	Coefficient (β)			Odds Ratio			*P*
	Observed	Bootstrap SE	95% CI	Observed	Bootstrap SE	95% CI	
HDL-C (≤1.4 mmol/L or not)	1.75	0.59	0.59-2.91	5.74	3.41	1.79-18.42	0.003
FPG (>4.99 mmol/L or not)	2.09	0.54	1.04-3.14	8.07	4.33	2.82-23.08	<0.001
Elevated-J-shaped trajectory (Yes/No)	1.51	0.63	0.28-2.73	4.52	2.83	1.33-15.40	0.016
Constant	-3.82	0.84	-5.12--2.53	0.01	0.01	0.00-0.07	<0.001

MetS=metabolic syndrome; SE=standard error; CI=confidence interval; HDL-C=high density lipoprotein cholesterol; FPG=fasting plasma glucose

Table S7. Univariate and multivariate linear regression analyses of the associations between the MetS-definition related components and systolic blood pressure during follow-up

Variable	B±SE	*β*	*P*
Univariate analysis			
HOMA-IR	3.23±0.57	0.31	<0.001
FPG (mmol/L)	6.08±1.10	0.30	<0.001
Triglycerides (mmol/L)	4.04±1.09	0.21	<0.001
HDL-C (mmol/L)	-3.27±2.63	-0.071	0.215
Waist circumference (cm)	0.20±0.10	0.172	0.045
Multivariate analysis			
HOMA-IR	3.23±0.58	0.31	<0.001
FPG (mmol/L)	5.95±1.10	0.29	<0.001
Triglycerides (mmol/L)	3.66±1.10	0.19	0.001

Multivariate analysis was carried out after adjustment of body mass index (at follow-up), duration of time after term, and maternal age at follow-up. Abbreviations: B=regression coefficient; SE=standard error; β=adjusted regression coefficient; MetS=metabolic syndrome; HOMA-IR= homeostatic model assessment of insulin resistance; FPG=fasting plasma glucose; HDL-C=high density lipoprotein cholesterol.

Table S8. Univariate and multivariate linear regression analyses of the associations between MetS-definition related variables and diastolic blood pressure during follow-up

Variable	B±SE	*β*	*P*
Univariate analysis			
HOMA-IR	2.33±0.43	0.30	<0.001
FPG (mmol/L)	4.30±0.83	0.28	<0.001
Triglycerides (mmol/L)	3.74±0.80	0.26	<0.001
HDL-C (mmol/L)	-3.74±1.96	-0.11	0.057
Waist circumference (cm)	0.14±0.08	0.15	0.073
Multivariate analysis			
HOMA-IR	2.35±0.44	0.30	<0.001
FPG (mmol/L)	4.21±0.83	0.28	<0.001
Triglycerides (mmol/L)	3.56±0.82	0.25	<0.001

Multivariate analysis was carried out after adjustment of body mass index (at follow-up), duration of time after term, and maternal age at follow-up. Abbreviations: B=regression coefficient; SE=standard error; β=adjusted regression coefficient; MetS=metabolic syndrome; HOMA-IR= homeostatic model assessment of insulin resistance; FPG=fasting plasma glucose; HDL-C=high density lipoprotein cholesterol.

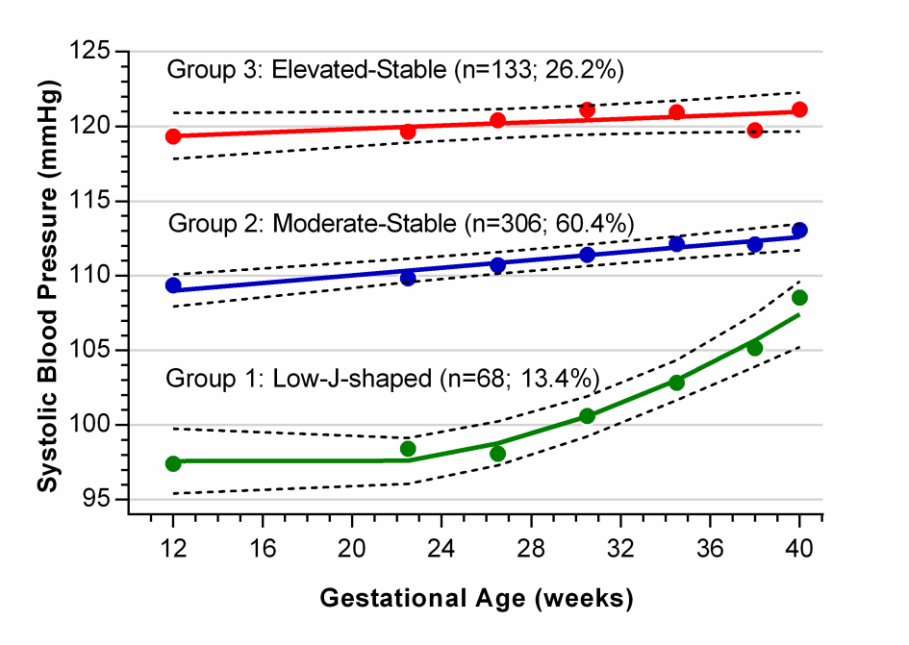

Figure S1. The SBP trajectory groups identified by latent class growth modeling*.

*The dash lines in panel A indicate 95% CI; For SBP, a 3-trajectory group model with quadratic, linear and linear specifications was identified for group 1(13.4%), group 2 (60.4%) and group 3 (26.2%), respectively. The group 1is in all above three models presented with a J-shaped change during pregnancy, i.e., a slight decrease in the second trimester followed by a steeper increase in the third trimester. Additionally the best-fit model for the group 3 of all three BP indexes was a linear specification with a stable/slightly incline pattern from 11^{+0}-13^{+6} weeks. For the moderate BP group (group 2), a linear specification was identified for SBP.

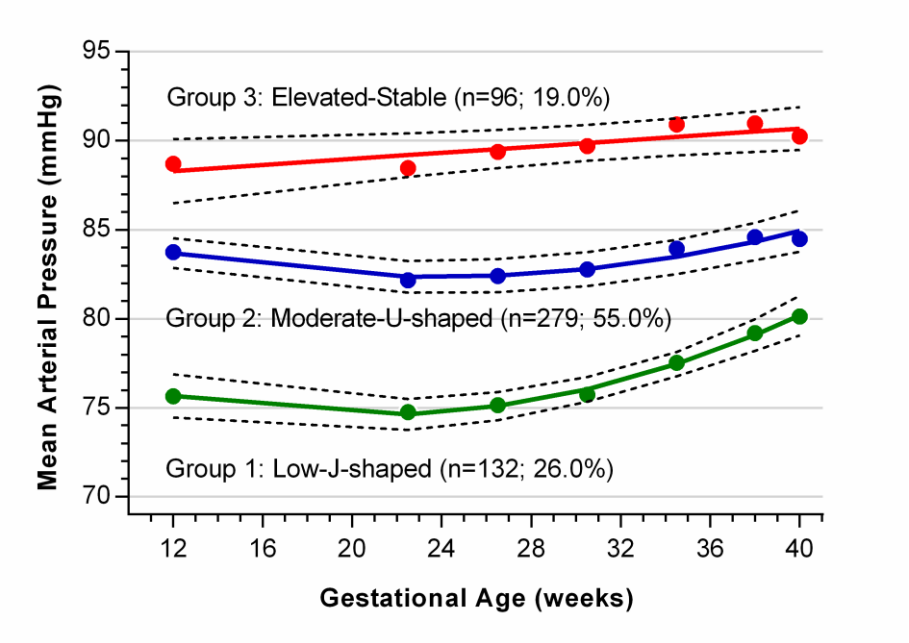

Figure S2. The MAP trajectory groups identified by latent class growth modeling*.

*The dash lines in panel A indicate 95% CI; For MAP, a 3-trajectory group model with quadratic, quadratic and linear specifications was identified for group 1(26.0%), group 2 (55.0%) and group 3 (19.0%), respectively. The group 1is in all above three models presented with a J-shaped change during pregnancy, i.e., a slight decrease in the second trimester followed by a steeper increase in the third trimester. Additionally the best-fit model for the group 3 of all three BP indexes was a linear specification with a stable/slightly incline pattern from 11^{+0}-13^{+6} weeks. For the moderate BP group (group 2), a quadratic specification was found in MAP.

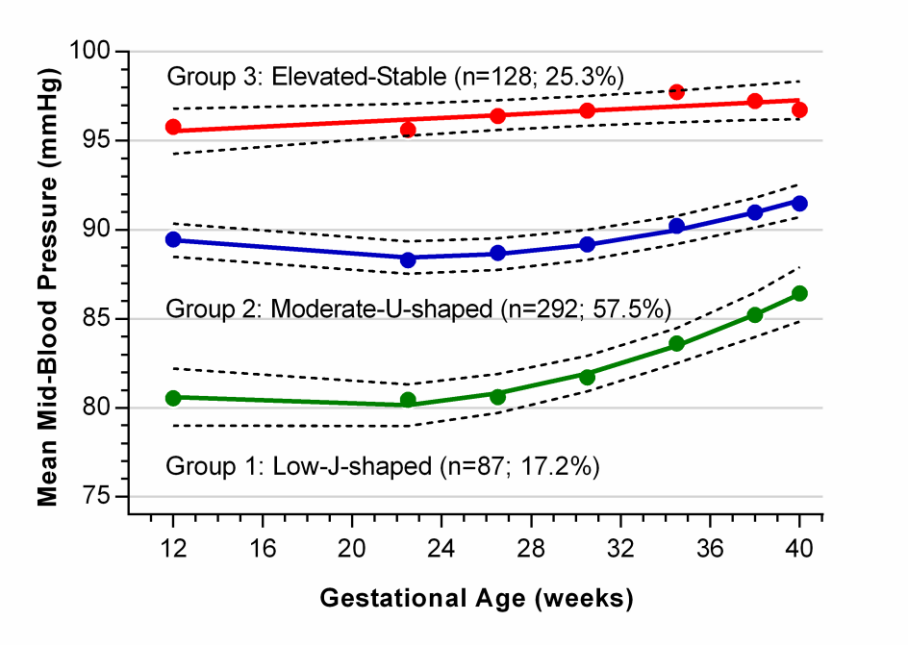

Figure S3. The mid-BP trajectory groups identified by latent class growth modeling*.

*The dash lines in panel A indicate 95% CI. For mid-BP, a 3-trajectory group with quadratic, quadratic and linear specifications for group 1(17.2%), group 2 (57.5%) and group 3 (25.3%), respectively. The group 1is in all above three models presented with a J-shaped change during pregnancy, i.e., a slight decrease in the second trimester followed by a steeper increase in the third trimester. Additionally the best-fit model for the group 3 of all three BP indexes was a linear specification with a stable/slightly incline pattern from 11^{+0}-13^{+6} weeks. For the moderate BP group (group 2), a quadratic specification was found in mid-BP.

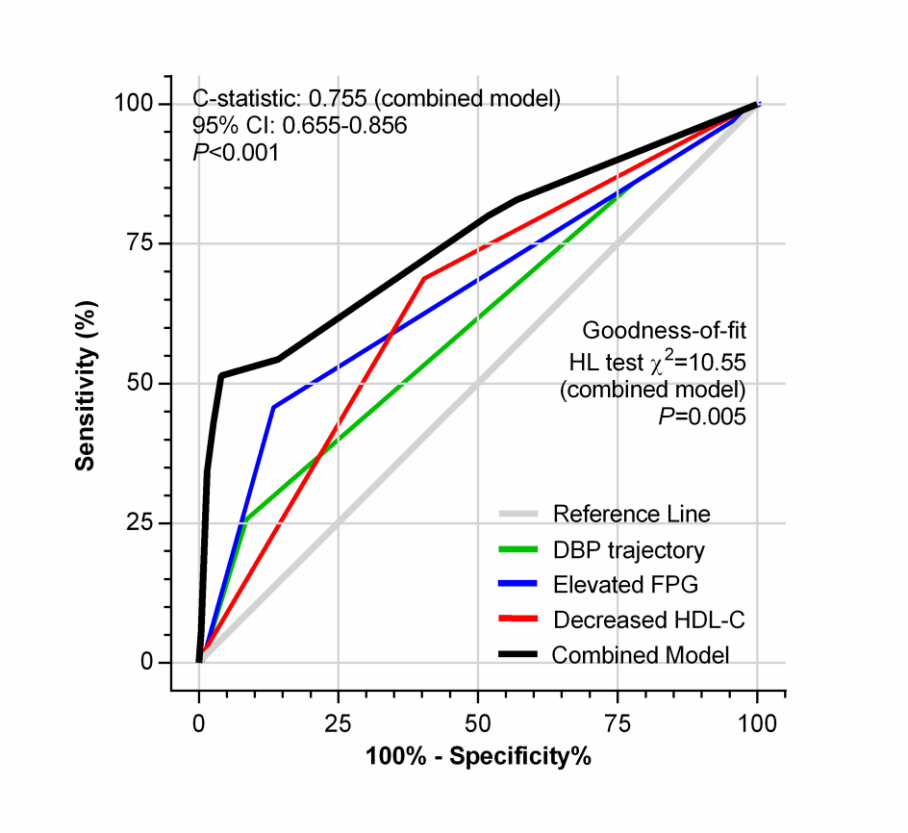

Figure S4. Receiver operating characteristic (ROC) curve for multiple logistic regression analyses incorporating DBP trajectories, FPG and HDL-C. The multiple logistic regression equation used to construct the ROC curve was as follows: logit(y) = -3.82 + (1.51×DBP_trajectory) + (1.75×HDL-C) + (2.09×FPG). CI=confidence interval. DBP=diastolic blood pressure; FPG=fasting plasma glucose; HDL-C=high density lipoprotein cholesterol; HL=Hosmer-Lemeshow. For cut-off values and ROC curve analyses for each variable, refer to **Table S5** and **Table S6**.