Published in final edited form as:

Obstet Gynecol. 2011 February ; 117(2 Pt 1): 225–232. doi:10.1097/AOG.0b013e3182075626.

Prior Preterm or Small-for-Gestational-Age Birth Related to Maternal Metabolic Syndrome

Janet M. Catov, PhD, MS, Rhiannon Dodge, MS, Jose-Miguel Yamal, PhD, James M. Roberts, MD, Linda B. Piller, MD, MPH, and Roberta B. Ness, MD, MPH

Departments of OB/GYN and Epidemiology, University of Pittsburgh, Pittsburgh, Pennsylvania; the Magee-Womens Research Institute, Pittsburgh, Pennsylvania; and The University of Texas Health Science Center at Houston School of Public Health, Houston, Texas

Abstract

OBJECTIVE—To estimate whether women who deliver small babies due to preterm birth or growth restriction have excess risk for cardiovascular disease and diabetes later in life.

METHODS—Eight years after pregnancy, we estimated the prevalence of metabolic syndrome and its components in a cohort study of women with prior preterm (preterm birth before 37 weeks, n=181) or small for gestational age (SGA), less than the tenth percentile, n=192) births, compared with women with term births (37 or more weeks, n=306). Women delivered at Magee-Womens Hospital in Pittsburgh, Pennsylvania, and those with preeclampsia or prepregnancy diabetes or hypertension were excluded. Women underwent a structured interview and fasting blood sampling.

RESULTS—Women were, on average, 8 years postpartum and 39 years old at evaluation. Women with a prior preterm birth had higher blood pressure, triglycerides, and LDL-cholesterol compared with those in a term control group. Women with prior SGA births were leaner and more likely to smoke compared with those with term births. Women with prior preterm birth had elevated risk of metabolic syndrome, adjusted for demographic, smoking and body size factors (23% preterm compared with 17% control group; odds ratio [OR] 1.76 [1.06, 2.80]). In women with a prior preterm birth, low HDL (11% preterm compared with 5% control group; OR 2.6 [1.2, 5.2]), hypertriglyceridemia (22% compared with 14%; OR 1.9 [1.2, 2.9]), and elevated glucose (24% compared with 19%; OR 1.5 [1.0, 2.3]) accounted for this excess metabolic syndrome. In women with SGA, the only element of metabolic syndrome that was aberrant was glucose metabolism.

CONCLUSION—Eight years after pregnancy, women with prior preterm or SGA births had evidence of metabolic syndrome compared with women with term births. Screening and intervention in these women after pregnancy may delay or prevent disease.

Women who deliver small babies due to preterm birth or growth restriction have excess risk for cardiovascular disease and diabetes.^{1–6} Several years after delivery, infant birth weight is inversely related to blood pressure, insulin resistance, and low-grade inflammation in

© 2011 by The American College of Obstetricians and Gynecologists.

Corresponding author: Janet M. Catov, PhD, MS, University of Pittsburgh, Department of OB/GYN, 300 Halket Street, Pittsburgh, PA 15213; catovjm@upmc.edu. .

Presented as part of a symposium at the Society for Epidemiologic Research Annual Meeting, June 23–25, 2010, Seattle, Washington.

Financial Disclosure

The authors did not report any potential conflicts of interest.

mothers.⁷⁻¹⁰ These data suggest that dysregulated metabolic factors may link preterm or small for gestational age deliveries to later life maternal disease.

The metabolic syndrome (MetS) is a cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus including hyperglycemia, hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol, and central adiposity. Presence of MetS is associated with a 2-fold increased risk for cardiovascular disease over 5–10 years compared with absence of the syndrome.¹¹ The MetS is common, has rising prevalence worldwide, and is both a public health and clinical problem. Our goal was to estimate the presence of MetS among women who had preterm or SGA births 4 to 12 years in the past. A secondary and thus more exploratory aim was to consider which individual MetS components may be perturbed in women with these pregnancy outcomes. We hypothesized that women with a history of preterm or SGA births would have evidence of the metabolic syndrome in the years after pregnancy compared with women with term, non-SGA births.

PARTICIPANTS AND METHODS

The Women and Infant Study of Healthy Hearts is a cohort study of cardiovascular risk factors assessed among women 4 to 12 years after delivery of singleton infants who were preterm, small for gestational age, or term non-SGA. The University of Pittsburgh Institutional Review Board approved all study procedures. Eligible women were those who gave birth between 1997 and 2002 at Magee-Womens Hospital in Pittsburgh, Pennsylvania, who did not have preeclampsia, prepregnancy hypertension, or diabetes. Of the 4,908 eligible women identified via a hospital electronic birth registry, 1,569 (32%) were able to be located via mail or phone and were screened. Of those screened, 702 women (45%) provided informed consent and were enrolled. A total of 817 women (52%) declined participation, and an additional 50 women were ineligible due to being currently pregnant or reporting a prepregnancy chronic condition. The 702 enrolled women were more likely to be African American (28.6% compared with 24.4%, $P=.02$) and were on average 0.5 years older (37.3 compared with 36.8 years, $P<.01$) than eligible women. We excluded women who reported their race or ethnicity as other than white or African American due to small numbers ($n=12$). We also excluded women with gestational diabetes ($n=11$), diagnosed according to Carpenter and Couston criteria,¹² given its well-established relation to later-life MetS. Final study population was 679 women.

Delivery characteristics were abstracted from hospital birth records including gestational age (based mainly on prenatal ultrasounds) and infant birth weight. Women were categorized as having delivered preterm (less than 37 weeks of gestation, $n=181$) or term, and the preterm group was further divided into those delivered at less than 34 weeks and at 34 to less than 37 weeks to describe severity. Preterm births were also categorized as spontaneous (following spontaneous premature membrane rupture or preterm labor) or medically indicated. In addition, women were categorized as having one or two or more preterm births. SGA infants were those less than the tenth percentile based on hospital specific nomograms accounting for gestational age, infant sex, and maternal race ($n=192$). The subset with a birth weight for gestational age at less than fifth percentile was separately assessed ($n=106$). Women with infants that were both preterm and SGA ($n=9$) were analyzed with the preterm group. Women with term, non-SGA infants (more than the tenth percentile) were the referent for all analyses ($n=306$).

Fasting blood samples were collected and all measurements were completed at the Nutrition Laboratory in the Department of Epidemiology at the University of Pittsburgh, which is Clinical Laboratory Improvement Amendments–certified and participates in the Centers for Disease Control and Prevention–National Heart, Lung and Blood Institute Lipid

Standardization and College of American Pathologists' Proficiency Programs. Total cholesterol, HDL, and triglycerides were measured using standard enzymatic procedures.¹³⁻¹⁵ LDL was estimated using the Friedewald calculation,¹⁶ and women with triglycerides more than 400 mg/dL were excluded from this analysis (n=12). The coefficient of variation ranged from 1.3% to 6.5%. Glucose was determined by an enzymatic determination,¹⁷ and the coefficient of variation was 1.8%. Insulin was measured using an radioimmunoassay procedure developed by Linco Research Inc (coefficient of variation 2.6%). Blood pressure was evaluated as the mean of three measurements following a 10-minute rest, and body mass index (BMI, calculated as weight (kg)/[height (m)]²) was calculated from measured height and weight. Waist circumference was assessed in centimeters with a tape measure at the umbilicus.

Several clinical criteria for MetS have been proposed. There is debate about the role of insulin resistance as a linking factor, and therefore we utilized criteria established by the World Health Organization (WHO) that requires presence of insulin resistance plus two additional risk factors,¹⁸ and the Joint Interim Statement criteria that harmonized those defined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III) and others.¹¹ The Joint Statement criterion does not include a direct measure of insulin resistance, but instead requires the presence of three of five possible risk factors. Presence of MetS was estimated using each of these criteria, and the risk of each individual component was also estimated (Table 1).

Women completed a structured interview to assess pregnancy and medical history, demographics, and lifestyle characteristics. Women reported the outcomes of all pregnancies before and following the index birth including gestational age and birth weight. Maternal race was categorized as white or African American. Smoking status and number of cigarettes smoked was assessed during pregnancy and at the postpartum study visit. Women also reported the first day of the last menstrual period, and days from menses to the study visit were calculated because some biomarkers are known to change during the menstrual cycle.^{19,20} Menopause was defined as having no menstrual periods during the previous 12 months; surgical removal of both ovaries; or age greater than 55 years accompanied by use of estrogen, hormone therapy, or a hysterectomy.

Weekly alcohol consumption was reported, and regular use was defined as consumption of some alcohol at least once a week.²¹ Physical activity was reported using the Paffenbarger Physical Activity Questionnaire²² and analyzed as total hours of physical activity expenditure per week (metabolic equivalent h/wk).²³ Gestational hypertension was defined as at least two blood pressures higher than 140/90 mm Hg after 20 weeks of gestation without proteinuria.

Characteristics of women with preterm, SGA, and term births were compared using χ^2 or Dunnett's test. Logistic regression was used to estimate the risk of developing MetS or its individual components according to a history of preterm or SGA birth, and women with term, non-SGA infants were the referent for all analyses.

To obtain noncollinear covariates for our logistic regression model, we used variable clustering to create groups of variables that are highly correlated with each other and describe the same feature.²⁴ We applied all covariates of interest to a hierarchical clustering graph, and found three significant variable clusters. The first included BMI and weight, both as continuous measures. The second cluster included education, income, and race (each measured categorically) and also age at index birth and at baseline (measured continuously). The third variable cluster included smoking during pregnancy, current smoking, and ever smoking (yes or no), as well as amount smoked during pregnancy, number of years smoked,

number of cigarettes smoked at baseline, and pack-years smoked among ever users (each measured continuously). We then used principal component analysis, with oblique rotation, to compute the linear combination of the variables within each cluster that explained the most amount of variance. The first principal component of each cluster can be thought of as a weighted sum of the clustered variables and hence the cluster representative, explaining 98% of the variance in the first cluster, 51% in the second, and 74% in the third. The three new variables were included in our final logistic regression models as covariates. Additional adjustment for gestational hypertension did not change any estimates and therefore this was not retained in the final models.

Analyses were performed with SAS 9.2 and R 2.6.2.

RESULTS

Women were evaluated, on average, 8.2 years postpartum (standard deviation [SD] 1.8). Women with prior preterm births were more likely to be older, to have had more than one preterm infant, to be of white race, and were marginally more likely to currently smoke compared with women with term births (Table 2). They also had higher mean blood pressures, triglycerides, and LDL cholesterol concentrations. Women with a prior SGA birth were leaner, with a lower mean BMI and a smaller mean waist circumference compared with women with term, non-SGA infants. They were also more likely to have smoked during pregnancy or at the study visit.

Women with prior preterm birth had excess risk of MetS according to the Joint Statement criteria after adjustment for confounders (OR 1.76, 95% confidence interval [CI] 1.06, 2.80; Table 1). They were more likely than women in the control group to have hypertriglyceridemia and elevated glucose concentrations. Although women with prior preterm births did not demonstrate MetS according to the WHO criteria, they were more than twice as likely as their term birth counterparts to have HDL cholesterol concentrations less than 35 mg/dL. Women with preterm births delivered at less than 34 weeks were two to three times more likely to have hypertriglyceridemia or low HDL cholesterol than women with term births, but they did not meet either clinical criteria for MetS. In contrast, women with preterm births delivered at 34 to less than 37 weeks had evidence of MetS according to the Joint Statement criteria (OR 1.82, 95% CI 1.05, 2.86).

The relation between medically induced preterm births (n=33) and MetS was stronger than that for spontaneous preterm births (n=148) after adjustment for confounders (OR 2.07 [0.83, 5.14]; OR 1.65 [0.96, 2.84], respectively). In contrast, there was no difference in the prevalence of MetS among women with one preterm birth compared with those with two or more (24% compared with 23%, respectively).

Women with prior SGA births less than the tenth percentile had marginally elevated risk of MetS compared with women with term, non-SGA births using the WHO criteria (OR 1.51, 95% CI 0.82, 2.60; Table 3). The only elevated component of MetS appeared to be fasting glucose concentrations less than 110 mg/dL, which was unmasked after adjustment for BMI (OR 2.30, 95% CI 0.92, 3.89). Women with SGA births less than the fifth percentile had 3.30 times the risk of elevated glucose (more than 110 mg/dL) compared with their counterparts with term, non-SGA births (95% CI 1.12, 7.85).

DISCUSSION

Women with a history of preterm or SGA births had evidence of metabolic syndrome on average 8 years after delivery. This association was strongest for women with prior preterm births, and these women had elevated glucose and abnormal lipids compared with women

with term births. Women with prior SGA births had elevated glucose, with no other MetS abnormalities apparent at an average age of 39 years. These results suggest that insulin resistance is present in women with preterm or SGA births, but the accompanying dyslipidemia may be present only in women with prior preterm births.

Lawlor et al reported that infant birth weight was inversely related to maternal insulin resistance in older women at a mean age of 68 years.⁹ MetS was detected in our study in young adulthood, at a time when these processes may be reversed or attenuated through relatively simple lifestyle interventions to delay or prevent onset of clinical disease.

In addition, relating offspring birth weight to insulin resistance, without distinguishing the underlying reasons that babies are born small, may mask what are important maternal metabolic sequelae. Our finding of abnormal lipids following preterm births is consistent with previous studies by our group and others demonstrating elevated lipids before²⁵ and during pregnancy among women who deliver preterm.^{26,27} Thus, pregravid dysregulated metabolic factors may contribute to preterm birth risk, persist in the postpartum period, and be related to excess risk many years later for cardiovascular disease and diabetes. There is debate about when to initiate lipid screening in young healthy women,²⁸ but our results suggest that women with prior preterm births could be considered high risk and thus benefit from screening in the decade following pregnancy.

Lipid metabolism was altered in women with either early or moderate preterm births in our study. In contrast, clinical evidence of MetS was only detected in women with preterm births delivered at 34 to less than 37 weeks. This is consistent with evidence that early preterm births have some distinct pathogeneses, such as infection,²⁹ that may be unrelated to later life metabolic aberrations. In addition, evidence of maternal MetS was strongest following medically induced preterm births and intermediate following spontaneous preterm births. Reasons for induced preterm births in our study were placenta previa or abruption, suspected growth restriction, maternal diseases other than hypertension, and other fetal or maternal conditions. Cases of preeclampsia were excluded from our study by design.

Our results indicate more modest metabolic aberrations among women following SGA births, with evidence only of glucose impairment in this group. One small study of 28 women with SGA births less than the fifth percentile reported evidence of altered lipids, inflammation, and endothelial activation 4 years postpartum compared with women in a control group matched on several factors, but not differences in glucose, insulin, or insulin resistance.⁸ Women in our study were on average 10 years older, were heavier, and were more likely to be multiparous, suggesting that the study populations are not comparable. Moreover, our larger study may have had more power to detect significant differences. Women with prior SGA births in our study were leaner compared with their counterparts with term births. Of note, elevated glucose in women with prior SGA births was only detected after accounting for BMI, raising the possibility of a metabolically obese, lean phenotype³⁰ that may be related to SGA births and later-life risk for cardiovascular disease.

Limitations of our study include modest enrollment of eligible women, which could impair generalizability. If replicated in other populations, however, our findings suggest that screening for MetS among young women with prior preterm or SGA births may identify a group at higher risk for cardiovascular disease and diabetes who might not otherwise be screened. The number of events for several MetS criteria in our study was small, and thus some estimates are imprecise. In addition, we did not account for multiple comparisons, as our main study outcome was the presence or absence of MetS. Strengths of our study include a large group of women with pregnancy data abstracted from hospital birth records

and body measurements, interview data, and fasting blood collected on average 8 years postpartum.

Our results indicate that women with a history of preterm or SGA births have evidence of MetS 4–12 years after delivery. Preterm birth in particular was associated with lipid and glucose abnormalities as well as presence of MetS. SGA births were associated with impaired glucose metabolism despite a leaner body composition in this group. If confirmed by other studies, our results suggest some divergent cardiovascular disease risk factors in women with preterm or SGA births. Screening women with these events in the decade following pregnancy may identify a group at elevated risk for the metabolic syndrome. Relatively simple diet and lifestyle interventions in women following preterm or SGA births may help delay or prevent onset of metabolic syndrome, cardiovascular disease, and diabetes.

Acknowledgments

Supported by National Institutes of Health grants R01HL076532 and K12 HD043441.

REFERENCES

1. Catov JM, Newman AB, Roberts JM, Kelsey SF, Sutton-Tyrrell K, Harris TB, et al. Preterm delivery and later maternal cardiovascular disease risk. *Epidemiology*. 2007; 18:733–9. [PubMed: 17917602]
2. Smith GD, Harding S, Rosato M. Relation between infants' birth weight and mothers' mortality: prospective observational study. *BMJ*. 2000; 320:839–40. [PubMed: 10731177]
3. Smith GD, Whitley E, Gissler M, Hemminki E. Birth dimensions of offspring, premature birth, and the mortality of mothers. *Lancet*. 2000; 356:2066–7. [PubMed: 11145495]
4. Smith GD, Sterne J, Tynelius P, Lawlor DA, Rasmussen F. Birth weight of offspring and subsequent cardiovascular mortality of the parents. *Epidemiology*. 2005; 16:563–9. [PubMed: 15951676]
5. Smith G, Pell JP, Walsh D. Pregnancy complications and maternal risk of ischaemic heart disease: a retrospective cohort study of 129,290 births. *Lancet*. 2001; 357:2002–6. [PubMed: 11438131]
6. Catov JM, Wu CS, Olsen J, Sutton-Tyrrell K, Li J, Nohr EA. Early or recurrent preterm birth and maternal cardiovascular disease risk. *Ann Epidemiol*. 2010; 20:604–9. [PubMed: 20609340]
7. Catov JM, Newman AB, Roberts JM, Sutton-Tyrrell KC, Kelsey SF, Harris T, et al. Association between infant birth weight and maternal cardiovascular risk factors in the health, aging, and body composition study. *Ann Epidemiol*. 2007; 17:36–43. [PubMed: 16843009]
8. Kanagalingam MG, Nelson SM, Freeman DJ, Ferrell WR, Cherry L, Lowe GDO, et al. Vascular dysfunction and alteration of novel and classic cardiovascular risk factors in mothers of growth restricted offspring. *Atherosclerosis*. 2009; 205:244–50. [PubMed: 19022445]
9. Lawlor DA, Davey Smith G, Ebrahim S. Birth weight of offspring and insulin resistance in late adulthood: cross sectional survey. *BMJ*. 2002; 325:359. [PubMed: 12183306]
10. Walker BR, McConnachie A, Noon JP, Webb DJ, Watt GC. Contribution of parental blood pressures to association between low birth weight and adult high blood pressure: cross sectional study. *BMJ*. 1998; 316:834–7. [PubMed: 9549456]
11. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JI, Donato KA, et al. Harmonizing the Metabolic Syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*. 2009; 120:1640–5. [PubMed: 19805654]
12. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. *Am J Obstet Gynecol*. 1982; 144:768–73. [PubMed: 7148898]

13. Allain CC, Poon LS, Chan CS, Richmond W, Fu PC. Enzymatic determination of total serum cholesterol. *Clin Chem.* 1974; 20:470–5. [PubMed: 4818200]
14. Bucolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. *Clin Chem.* 1973; 19:476–82. [PubMed: 4703655]
15. Warnick GR, Albers JJ. A comprehensive evaluation of heparin-manganese precipitation procedure for estimating high density lipoprotein cholesterol. *J Lipid Res.* 1978; 19:65–76. [PubMed: 202660]
16. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem.* 1972; 18:499–502. [PubMed: 4337382]
17. Bondar RJ, Mead DC. Evaluation of glucose-6 phosphate dehydrogenase from *Leuconostoc mesenteroides* in the hexokinase method for determining glucose in serum. *Clin Chem.* 1974; 20:586–90. [PubMed: 4363766]
18. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med.* 1998; 15:539–53. [PubMed: 9686693]
19. Bingley CA, Gitau R, Lovegrove JA. Impact of menstrual cycle phase on insulin sensitivity measures and fasting lipids. *Horm Metab Res.* 2008; 40:901–6. [PubMed: 18726830]
20. Valdes CT, Elkind-Hirsch KE. Intravenous glucose tolerance test-derived insulin sensitivity changes during the menstrual cycle. *J Clin Endocrinol Metab.* 1991; 72:642–6. [PubMed: 1997519]
21. Caetano R, Cunradi CB, Clark CL, Schafer J. Intimate partner violence and drinking patterns among white, black, and Hispanic couples in the U.S. *J Subst Abuse.* 2000; 11:123–38. [PubMed: 10989773]
22. Sesso HD, Paffenbarger RS, Ha T, Lee IM. Physical activity and cardiovascular disease risk in middle-aged and older women. *Am J Epidemiol.* 1999; 150:408–16. [PubMed: 10453817]
23. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc.* 2000; 32(9 suppl):S498–516. [PubMed: 10993420]
24. Harrell, FE, Jr.. Regression modeling strategies. Springer; New York (NY): 2001.
25. Catov JM, Ness RB, Wellons MF, Jacobs DR, Roberts JM, Gunderson EP. Prepregnancy lipids related to preterm birth risk: the coronary artery risk development in young adults study. *J Clin Endocrinol Metab.* 2010; 95:3711–8. [PubMed: 20501685]
26. Catov JM, Bodnar LM, Kip KE, Hubel C, Ness RB, Harger G, et al. Early pregnancy lipid concentrations and spontaneous preterm birth. *Am J Obstet Gynecol.* 2007; 107:610e1–7. [PubMed: 18060950]
27. Edison RJ, Berg K, Remaley A, Kelley R, Rotimi C, Stevenson RE, et al. Adverse birth outcome among mothers with low serum cholesterol. *Pediatrics.* 2007; 120:723–33. [PubMed: 17908758]
28. Kuklina EV, Yoon PW, Keenan NL. Trends in high levels of low-density lipoprotein cholesterol in the United States, 1999–2006. *JAMA.* 2009; 302:2104–10. [PubMed: 19920234]
29. Goldenberg RL, Hauth JC, Andrews WW. Intrauterine infection and preterm delivery. *N Engl J Med.* 2000; 342:1500–7. [PubMed: 10816189]
30. Goodpaster BH, Krishnaswami S, Resnick H, Kelley DE, Haggerty C, Harris TB, et al. Association between regional adipose tissue distribution and both type 2 diabetes and impaired glucose tolerance in elderly men and women. *Diabetes Care.* 2003; 26:372–9. [PubMed: 12547865]

Table 1

Prevalence of the Metabolic Syndrome According to Preterm Birth Status

	Preterm (Less Than 37 wk)		Preterm 34 to Less Than 37 wk		Preterms (Less Than 34 wk)	
	Preterm (n=181)	Control Group (n=306)	Adjusted OR (95% CI) *	Preterm (n=126)	Adjusted OR (95% CI) *	Preterm (n=55)
Joint Statement criteria						
Metabolic syndrome	42 (23)	53 (17)	1.76 (1.06–2.80)	30 (24)	1.82 (1.05–2.86)	12 (22)
Fasting blood glucose 100 mg/dL or higher [†]	44 (24)	58 (19)	1.50 (0.98–2.30)	30 (24)	1.46 (0.89–2.38)	14 (25)
Triglycerides 150 mg/dL or higher [†]	39 (22)	42 (14)	1.89 (1.15–2.89)	25 (20)	1.69 (0.98–2.80)	14 (25)
HDL cholesterol less than 50 mg/dL [†]	65 (36)	113 (37)	1.05 (0.69–1.52)	46 (37)	1.06 (0.68–1.62)	19 (35)
BP 130/85 mmHg or higher [†]	19 (11)	23 (7)	1.55 (0.82–2.83)	14 (11)	1.69 (0.90–3.28)	5 (9)
Waist circumference more than 88 cm	98 (54)	175 (57)	0.99 (0.60–1.62)	71 (56)	1.18 (0.67–1.97)	27 (49)
Modified WHO criteria						
Metabolic syndrome	19 (11)	32 (10)	1.15 (0.65–2.05)	13 (11)	1.12 (0.59–2.15)	6 (11)
Fasting insulin more than 75th percentile [†] or...	54 (30)	101 (33)	0.92 (0.60–1.43)	39 (31)	0.98 (0.62–1.59)	15 (27)
Fasting blood glucose 110 mg/dL or higher [†]	8 (5)	10 (3)	1.60 (0.65–4.10)	5 (4)	1.45 (0.50–4.10)	3 (5)
Triglycerides 150 mg/dL [†] or...	39 (22)	42 (14)	1.89 (1.15–2.89)	25 (20)	1.69 (0.98–2.80)	14 (25)
HDL cholesterol less than 35 mg/dL [†]	19 (11)	15 (5)	2.55 (1.22–5.18)	12 (10)	2.20 (1.00–4.81)	7 (13)
BP 140/90 mmHg or higher [†]	13 (7)	15 (5)	1.55 (0.74–3.20)	10 (8)	1.79 (0.79–3.98)	3 (6)
Waist circumference 80 cm or more	137 (76)	233 (76)	1.12 (0.67–1.86)	91 (72)	0.89 (0.50–1.58)	46 (84)

OR, odds ratio; CI, confidence interval; HDL, high-density lipoprotein; BP, blood pressure; WHO, World Health Organization.

* Models are adjusted for socioeconomic status cluster (age at baseline, age at index birth, race, education, income), body size cluster (body mass index and weight at baseline), and smoking cluster (smoking during pregnancy [yes or no], amount smoked during pregnancy, current or not current smoking, ever smoking [yes or no], number of cigarettes smoked, number of years smoked [among ever smokers]).

[†] Either the condition for each metabolic criteria is met, or the individual is on medication for the specific condition (eg, blood pressure).

[‡] The 75th percentile cutoff for fasting insulin in our study population was 12 international units/mL.

Table 2

Characteristics and Clinical Variables According to Pregnancy Outcome

	Term SGA (n=192)	P*	Preterm (n=181)	P*	Term AGA (n=306)
Index pregnancy (1997–2002)					
Age (y)	29.1±6.6	.55	30.5±6.8	<.01	28.5±6.9
Prepregnancy weight (kg)	61.4±15.1	<.01	65.3±13.2	.76	66.3±18.6
African American	46 (24)	.03	46 (26)	.06	103 (34)
Gestational age (wk)	39.3±1.2	.99	34.0±2.5	<.01	39.3±1.1
Birth weight (g)	2,601.6±270.9	<.01	2,373.2±605.4	<.01	3,275.2±400.9
Multiparous	155 (81)	.03	152 (84)	.34	269 (88)
First born-index pregnancy	76 (40)	.89	70 (39)	.74	123 (40)
Additional preterm births	30 (16)	.45	54 (30)	<.01	38 (12)
Gestational hypertension	2 (1)	.43	2 (1)	.47	6 (2)
Smoking during pregnancy	59 (36)	<.01	30 (19)	.61	59 (21)
Study visit (2005–2009)					
Time since index pregnancy (y)	8.2±1.8	.61	8.5±1.7	.18	8.0±1.7
Age (y)	37.3±7.2	.45	39.0±7.0	<.01	36.5±7.4
Tobacco use-current	72 (38)	.01	60 (33)	.08	76 (25)
Pack-years smoked [†]	5.4±7.5	.44	4.6±6.5	.93	4.2±5.9
Body mass index (kg/m ²)	26.0±6.3	<.01	27.3±6.6	.57	27.8±7.0
Waist circumference (cm)	87.8±13.9	<.01	91.7±15.1	.81	92.5±15.8
Oral contraceptive use	31 (16)	.59	18 (10)	.16	44 (14)
Menopause	5 (3)	.09	22 (12)	.01	18 (6)
Alcohol consumption [†]	75 (39)	.67	61 (34)	.82	108 (35)
Physical activity (MET-h/wk)	13.1±17.8	.39	12.1±8.0	.19	15.9±32.8
Education		.97		.58	
Less than high school	14 (7)		7 (4)		20 (7)
High school	52 (27)		49 (27)		88 (29)
College	101 (53)		99 (55)		159 (52)
More than college	25 (13)		26 (14)		39 (13)
Income		.03			

	Term SGA (n=192)	P*	Preterm (n=181)	P*	Term AGA (n=306)
Less than \$20,000	41 (21)		37 (20)		80 (26)
\$20,000 to less than 50,000	49 (26)		50 (28)		60 (20)
\$50,000 to less than \$100,000	61 (32)		53 (29)		93 (30)
More than \$100,000	30 (16)		28 (15)		62 (20)
Do not know	11 (6)		13 (7)		11 (4)
Insurance		.64		<.01	
Medicaid	39 (20)		19 (11)		77 (25)
Medicare	4 (2)		5 (3)		8 (3)
Private	139 (73)		146 (81)		205 (67)
None	10 (5)		11 (6)		16 (5)
Menstrual cycle phase		.34		.09	
Fewer than 14 days of menses	80 (42)		76 (42)		147 (48)
14 or more days of menses	112 (58)		105 (58)		159 (52)
Family history					
Hypertension	105 (55)	.58	109 (60)	.51	175 (57)
Diabetes	10 (5)	.64	9 (5)	.57	19 (6)
Heart disease	59 (31)	.09	54 (30)	.15	73 (24)
Stroke	21 (11)	.77	24 (13)	.63	36 (12)
Toxemia	18 (9)	.54	18 (10)	.69	34 (11)
Clinical variables					
Systolic BP (mmHg)	105.9±14.3	.69	109.0±12.3	.05	106.7±10.4
Diastolic BP (mmHg)	68.8±10.7	.29	71.5±7.8	.04	69.8±8.3
HDL cholesterol (mg/dL)	57.8±13.8	.59	57.5±15.1	.76	56.6±14.2
LDL cholesterol (mg/dL)	109.8±33.2	.96	118.0±30.1	<.01	109.1±33.1
Triglycerides (mg/dL)	102.7±56.7	.78	112.2±66.2	.04	99.4±54.0
Insulin (international units/mL)	10.4±5.9	.42	11.1±6.2	.99	11.1±6.8
Glucose (mg/dL)	93.3±11.2	.84	93.1±16.8	.92	92.6±11.9

SGA, small for gestational age; AGA, appropriate for gestational age; MET, metabolic equivalent; BP, blood pressure; HDL, high-density lipoprotein; LDL, low-density lipoprotein. Data are mean±standard deviation or n (%) unless otherwise specified.

* Dunnett's test for means and χ^2 test for categorical variables, comparing women with term SGA or preterm birth with women in a control group separately.

[†] Pack years smoked among ever users (at least 200 cigarettes in lifetime); regular alcohol use was defined as drinking beer, wine, or liquor at least once a week.

Prevalence of Metabolic Syndrome Among Women With Small-for-Gestational-Age Births Compared With Women With Non-Small-for-Gestational-Age Term Births

Table 3

	SGA Less Than 10th Percentile		SGA 5th to Less Than 10th Percentile		SGA Less Than 5th Percentile	
	SGA Less Than 10th (n=192)	Control Group (n=304)	Adjusted OR (95% CI)*	(n=86)	Adjusted OR (95% CI)*	(n=106)
Joint Statement criteria						
Metabolic syndrome	29 (15)	53 (17)	1.15 (0.68–1.89)	10 (12)	0.78 (0.36–1.67)	19 (18)
Fasting blood glucose 100 mg/dL or higher	40 (21)	58 (19)	1.30 (0.80–1.92)	15 (17)	1.08 (0.59–1.96)	25 (24)
Triglycerides 150 mg/dL or higher	32 (17)	42 (14)	1.37 (0.79–2.20)	11 (13)	1.05 (0.50–2.08)	21 (20)
HDL cholesterol less than 50 mg/dL	65 (34)	113 (37)	1.01 (0.66–1.50)	32 (37)	1.08 (0.62–1.88)	33 (31)
BP 130/85 mmHg or higher	17 (9)	23 (7)	1.50 (0.78–2.79)	5 (6)	1.02 (0.35–2.58)	12 (11)
Waist circumference more than 88 cm	83 (43)	175 (57)	0.76 (0.45–1.29)	37 (43)	0.65 (0.32–1.29)	46 (43)
Modified WHO Criteria						
Metabolic syndrome	21 (11)	32 (10)	1.51 (0.82–2.60)	9 (11)	1.38 (0.61–3.12)	12 (11)
Fasting insulin more than 75th percentile OR	47 (24)	101 (33)	0.99 (0.62–1.59)	24 (28)	1.10 (0.60–1.98)	23 (22)
Fasting blood glucose 110 mg/dL or higher	10 (5)	10 (3)	2.30 (0.92–3.89)	3 (3)	1.50 (0.42–5.29)	7 (7)
Triglycerides more than 150 mg/dL OR	32 (17)	42 (14)	1.37 (0.79–2.20)	11 (13)	1.05 (0.50–2.08)	21 (20)
HDL cholesterol less than 35 mg/dL	7 (4)	15 (5)	0.98 (0.40–2.54)	6 (7)	1.83 (0.72–4.59)	1 (1)
BP 140/90 mmHg or higher	10 (5)	15 (5)	1.39 (0.60–2.98)	5 (6)	1.50 (0.56–4.21)	5 (5)
Waist circumference 80 cm or more	130 (68)	233 (76)	1.01 (0.62–1.66)	59 (69)	0.99 (0.56–1.88)	71 (67)

SGA, small for gestational age; OR, odds ratio; CI, confidence interval; HDL, high-density lipoprotein; BP, blood pressure; WHO, World Health Organization. Data are n (%) unless otherwise specified.

* Models are adjusted for SES cluster (age at baseline, age at index birth, race, education, income), body size cluster (body mass index and weight at baseline), and smoking cluster (smoking during pregnancy [yes or no], amount smoked during pregnancy, current or not current smoking, ever smoking [yes or no], number of cigarettes smoked, number of years smoked [among ever smokers]).