

# Asthma During Pregnancy

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**OBJECTIVE:** To determine neonatal and maternal outcomes stratified by asthma severity during pregnancy by using the 1993 National Asthma Education Program Working Group on Asthma and Pregnancy definitions of asthma severity. The primary hypothesis was that moderate or severe asthmatics would have an increased incidence of delivery at <32 weeks of gestation compared with nonasthmatic controls.

**METHODS:** This was a multicenter, prospective, observational cohort study conducted over 4 years at 16 university hospital centers. Asthma severity was defined according to the National Asthma Education Program Working Group on Asthma and Pregnancy classification and modified to

include medication requirements. This study had 80% power to detect a 2- to 3-fold increase in delivery less than 32 weeks of gestation among the cohort with the moderate or severe asthma compared with controls. Secondary outcome measures included obstetrical and neonatal outcomes.

**RESULTS:** The final analysis included 881 nonasthmatic controls, 873 with mild asthma, 814 with moderate, and 52 with severe asthma. There were no significant differences in the rates of preterm delivery less than 32 weeks (moderate or severe 3.0%, mild 3.4%, controls 3.3%;  $P = .873$ ) or less than 37 weeks of gestation. There were no significant differences for neonatal outcomes except discharge diagnosis of neonatal sepsis among the mild group compared with controls, adjusted odds ratio 2.9, 95% confidence interval 1.2, 6.8. There were no significant differences for maternal complications except for an increase in overall cesarean delivery rate among the moderate-or-severe group compared with controls (adjusted odds ratio 1.4, 95% confidence interval 1.1, 1.8).

**CONCLUSION:** Asthma was not associated with a significant increase in preterm delivery or other adverse perinatal outcomes other than a discharge diagnosis of neonatal sepsis. Cesarean delivery rate was increased among the cohort with moderate or severe asthma. (*Obstet Gynecol* 2004;103:5-12. © 2004 by The American College of Obstetricians and Gynecologists.)

**LEVEL OF EVIDENCE:** II-2

Asthma is probably the most common potentially serious medical complication of pregnancy. A recent study suggests that nearly 6% of pregnant women have asthma, and the most recent asthma surveillance data suggest that approximately 9% of the U.S. population report a physician diagnosis of asthma during their lifetime.<sup>1-3</sup> In general, the prevalence and morbidity from asthma are increasing.<sup>1,3</sup>

There have been few large prospective studies of asthma during pregnancy. Moreover, previous studies

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have a number of methodological inadequacies, including low power; poor control for confounders; little information regarding asthma severity, management, or control; and time frames not reflective of current management. Existing studies on the effects of asthma on pregnancy outcomes have had inconsistent results in regard to perinatal mortality, prematurity, low birth weight, neonatal hypoxia, cesarean delivery, hemorrhage, and preeclampsia.<sup>3-18</sup> Asthma has been associated with preterm delivery in some,<sup>4-9</sup> but not all studies.<sup>3,10-16</sup> Prematurity is a leading cause of perinatal mortality and long-term neurological morbidity in children, with very early preterm births (less than 32 weeks of gestation) accounting for most of the morbidity and mortality.<sup>19</sup> Perlow et al<sup>8</sup> in 1992 reported a case-control study of 130 controls and 81 women with asthma, 31 of whom required long-term oral corticosteroids and 50 who had nonsteroid medication-dependent asthma. They found a 7.7-fold increase of preterm delivery less than 37 weeks and a 4-fold increase of deliveries less than 32 weeks of gestation among those with asthma compared with controls.

In 1993, under the auspices of the National Asthma Education Program of the National, Heart, Lung, and Blood Institute, a working group on asthma and pregnancy defined mild, moderate, and severe asthma according to symptoms and pulmonary function criteria in untreated patients.<sup>20</sup> The relationship between National Asthma Education Program severity classification and pregnancy outcomes has not been reported.<sup>3-18</sup>

The 1993 National Asthma Education Program guidelines did not discuss classification of asthma severity for women who were already receiving medications for their asthma.<sup>20</sup> We previously reported asthma morbidity among the women in this study<sup>21</sup> and modified National Asthma Education Program asthma severity criteria to include medication use. Women with moderate asthma solely on the basis of requiring daily asthma medications had significantly more asthma exacerbations than those with mild asthma, but they did not have significantly more exacerbations than those with moderate asthma based on symptoms and measurements of forced expiratory volume of air expired in 1 second (FEV<sub>1</sub>). Women with severe asthma solely on the basis of requiring daily oral corticosteroids had significantly more exacerbations than those with moderate asthma, but they did not have significantly more exacerbations than those with severe asthma based on FEV<sub>1</sub>.<sup>21</sup>

The purpose of this study was to determine pregnancy outcomes stratified by asthma severity in a contemporary cohort of asthmatic women. The primary objective was to determine the frequency of preterm delivery at less than 32 weeks of gestation and other perinatal

outcomes among those with asthma compared with non-asthmatic controls.

## METHODS

This was a prospective observational cohort study that was sponsored by the National Institute of Child Health and Human Development and the National, Heart, Lung, and Blood Institute. The study was conducted at 16 centers of the Maternal-Fetal Medicine Units Network of the National Institute of Child Health and Human Development. The target enrollment was 900 women with mild asthma, 900 with moderate or severe (moderate-severe) asthma, and 900 control participants. Smoking status is an important determinant of both asthma morbidity and perinatal outcome. To avoid a disproportion of frequency of the smokers in the three cohorts, the control and mild-asthma cohorts were prospectively balanced in terms of the proportions of smoking status (any in the past week) with the moderate-severe cohort. Controls were also prospectively balanced for proportion of African-American ethnicity with the moderate-severe cohort. Smoking status and asthma severity were determined upon enrollment. Recruitment began in December 1994 and ended in March 1999. Case finding was by questioning all obstetric patients about ever having physician-diagnosed asthma. Informed, written consent was obtained from all participants, and each institution's local Institutional Review Board approved the study. Exclusion criteria at enrollment included the following: known multiple gestation, intrauterine fetal demise, major congenital abnormalities, active pulmonary disease other than asthma, inability to schedule an ultrasound for gestational age confirmation, gestational age 26 weeks or more at intake, or participation in the asthma randomized clinical trial or other interventional studies. In addition to these exclusion criteria, any woman who had ever had a physician diagnosis of asthma was excluded from the control group.

We collected demographic, social, and medical information, including ethnicity, age, smoking status (any in the previous week), prepregnancy weight, miscarriage/abortion, history of preterm delivery, insurance type, education, marital status, and chronic hypertension defined as either systolic more than 140 mm Hg or diastolic blood pressure more than 90 mm Hg on at least two occasions 4 or more hours apart when not pregnant or at less than 20 weeks of gestation or if the patient was on an antihypertensive medication when not pregnant or at less than 20 weeks of gestation. Spirometry (more than 4 hours postbronchodilator) was performed on participants with asthma at enrollment. Measurements of



**Table 1.** Classification of Asthma Severity

Classification of asthma	Criteria
Mild	All of the following: Asthma symptoms in the prior 6 months Asthma symptoms fewer than 8 days in prior 4 weeks (except with URI) FEV <sub>1</sub> ≥ 80% predicted Not taking daily asthma medications*
Moderate	Any of the following: Asthma symptoms on 8 or more days during the prior 4 weeks not attributable to a URI FEV <sub>1</sub> 60–79% predicted Use of one or more daily asthma medications*
Severe	Any of the following: FEV <sub>1</sub> < 60% predicted Use of daily or every other day oral corticosteroids for 4 weeks prior to enrollment

FEV<sub>1</sub> = forced expiratory volume of air expired in 1 second, measured at the time of enrollment > 4 hours post bronchodilator.

\* Daily medications included 2 puffs per day of inhaled  $\beta$  agonist, cromolyn, nedocromil, inhaled steroids, or 4 puffs per day of ipratropium or 1 dose per day of theophylline. Patients on regular oral corticosteroids were classified as severe irrespective of other criteria.

FEV<sub>1</sub> were made while the patient was standing after a maximal inspiration. To standardize spirometry techniques, all centers used Collins Stead-Well (Braintree, MA) dry-seal volume displacement spirometers, and all research nurses underwent a training and quality review program.

On each monthly study visit, an FEV<sub>1</sub> was obtained, and information regarding symptom frequency, asthma medication use, and the occurrence of asthma exacerbations was recorded. An exacerbation was defined as asthma symptoms (cough, dyspnea, or wheezing) severe enough to result in a medical intervention, including hospitalization, unscheduled visits (physician office or emergency department), and/or treatment with oral corticosteroids among subjects who were not already taking regular oral corticosteroids.

The classification of asthma severity was determined upon enrollment in the study. As we previously reported<sup>21</sup> and for the purposes of the current study, the National Asthma Education Program definitions of asthma severity were modified to include medication use (Table 1). Daily medication was defined as at least 2 puffs per day of inhaled  $\beta$ -agonist, cromolyn, nedocromil, or inhaled steroids, or at least 4 puffs per day inhaled ipratropium, or at least 1 dose per day of theophylline. Regular oral corticosteroid use was defined as daily or every other day dosing for at least 4 weeks before entry in the study.

The gestational age at the time of randomization was determined from the last menstrual period if it correlated with the first ultrasound. Dating was based upon first ultrasound if the last menstrual period estimate varied by more than 7 days from the ultrasound gestational age estimate if the first ultrasound was performed less than 20 weeks of gestation or more than 14 days if the first ultrasound was performed at or after 20 weeks of gestation.

The primary hypothesis was that the cohort with moderate-severe asthma would have an increased incidence of delivery at less than 32 weeks of gestation compared with nonasthmatic controls.<sup>8</sup> From previous studies, we estimated that the rate of preterm delivery at less than 32 weeks would be between 2% and 3%.<sup>22</sup> We felt that a 2- to 3-fold increase of preterm delivery among the moderate-severe cohort would be plausible and clinically relevant. We estimated that a sample size of 900 per group would be sufficient, with power of at least 80%, 2-sided type I error of 0.05, and allowing for a loss to follow-up rate of as much as 10%.

Secondary analyses included the incidence of gestational diabetes, preeclampsia, premature preterm rupture of membranes, induced for fetal indication, chorioamnionitis, oligohydramnios, cesarean delivery for fetal distress, total cesarean delivery, wheezing during labor, gestational age, preterm delivery (less than 37 weeks), labor duration, postpartum hemorrhage (more than 500 mL for vaginal delivery or more than 1,000 mL for cesarean delivery), birth weight, small for gestational age (less than 10th percentile, Brenner et al<sup>23</sup>), perinatal mortality, hyaline membrane disease, bronchopulmonary dysplasia, discharge diagnosis of neonatal sepsis, major congenital anomalies, patent ductus arteriosus, neonatal intensive care unit admission, intraventricular hemorrhage, necrotizing enterocolitis, and transient tachypnea of newborn. These data were obtained at postpartum chart reviews.

The Biostatistics Center of George Washington University maintained the data and performed the statistical analysis using SAS 8.2 (SAS Institute, Cary, NC) statistical software. The data were analyzed by using Kruskal-Wallis for continuous variables and  $\chi^2$  test and logistic regression analysis for dichotomous variables. Logistic regression covariates included asthma severity, previous preterm delivery, smoking status, African American versus other race, previous elective or spontaneous abortion, type of insurance, and minimum of high school education. For sparse outcomes, a reduced covariate set consisting of the first 4 covariates was used. Body mass index and oral corticosteroid use were also covariates for the model for gestational diabetes. Logistic regression results are reported as odds ratios and 95%



**Table 2.** Demographic and Baseline Information

	Moderate-severe ( <i>N</i> = 866)	Mild ( <i>N</i> = 873)	Control ( <i>N</i> = 881)	Overall <i>P</i>
Race				.002
African American	447 (51.6)	518 (59.3)	458 (52.0)*	
Caucasian	325 (37.5)	269 (30.8)	324 (36.8)	
Hispanic	77 (8.9)	78 (8.9)	74 (8.4)	
Other	17 (2.0)	8 (0.9)	25 (2.8)	
Age (y)	24.2 ± 6.1	22.4 ± 5.3	24.8 ± 6.1	< .001
Mean gestational age at enrollment (wk)	18.9 ± 4.8	18.1 ± 4.9	19.8 ± 4.3	< .001
Previous preterm delivery	142 (16.4)	111 (12.7)	136 (15.4)	.081
Previous miscarriages/abortions	363 (41.9)	323 (37.0)	345 (39.2)	.110
At least 12 years of schooling	522 (60.3)	509 (58.3)	584 (66.4)	.002
Smoked at enrollment	162 (18.7)	164 (18.8)	166 (18.8)	.998
Chronic hypertension	46 (5.3)	23 (2.6)	39 (4.4)	.017
Mean prepregnancy body mass index	27.9 ± 7.9	27.3 ± 7.6	26.5 ± 7.1	.002
Married	300 (34.6)	213 (24.4)	343 (38.9)	< .001
Insurance				.001
Government	680 (78.5)	702 (80.4)	644 (73.1)	
Private	136 (15.7)	100 (11.4)	164 (18.6)	
None	50 (5.8)	71 (8.1)	73 (8.3)	

Data presented as *N* (%) or mean ± standard deviation.

\* Not significant compared with moderate severe cohort, *P* = .764.

confidence intervals (95% CIs) with the control group as the referent. Significance was defined at *P* < .05 without correction for multiple comparisons.

## RESULTS

A total of 2,171 patients with asthma were asked to enroll in the study; 359 (16.5%) declined participation. We recruited 906 women with mild asthma, 906 with moderate-severe asthma, and 928 controls. One hundred twenty (4.4%) patients were lost to follow-up. Compared with the cohort remaining in the study, women lost to follow-up were significantly different with respect to age (24 ± 6 years versus 22 ± 5 years; *P* = .002), weeks of gestational age at enrollment (19 ± 5 weeks versus 18 ± 5 weeks; *P* = .006), and government insurance (77.3% versus 84.2%; *P* = .014). Losses to follow-up did not affect the relative balance of smoking or ethnicity among the 3 cohorts. The final analysis included 881 controls, 873 with mild asthma, and 866 with moderate-severe asthma. Of the moderate-severe cohort, 52 (6.0%) were classified as having severe asthma. Demographic and baseline information and length of follow-up by initial severity group are presented in Table 2. There were significant differences in ethnicity, age, level of education, body mass index, marital status, chronic hypertension, and type of insurance. The mean gestational age at study entry was 19.3 ± 4.7 weeks. Women with moderate-severe asthma were treated with the following medications during the 4 weeks before enrollment: inhaled β-agonist (*n* = 377, 41.6%), inhaled corticosteroids (*n* =

194, 21.4%), theophylline (*n* = 54, 6.0%), oral corticosteroids (*n* = 18, 2.0%), inhaled ipratropium (*n* = 19, 2.1%), inhaled cromolyn or inhaled nedocromil (*n* = 15, 1.7%), and oral β-agonist (*n* = 11, 1.2%). Patients could be on more than one medication. During this study, 4 women were intubated for asthma exacerbations, but there were no maternal deaths.

Patients with mild asthma had an asthma exacerbation rate of 12.6% (*n* = 110), and asthma hospitalization rate of 2.3% (*n* = 20).<sup>21</sup> Those with moderate asthma had an exacerbation rate of 25.7% (*n* = 209) and hospitalization rate of 6.8% (*n* = 55). Severe asthmatics had exacerbation and hospitalization rates of 51.9% (*n* = 27) and 26.9% (*n* = 14), respectively. During this study, 23% of women had an improvement in asthma severity, and 30.3% had an increase of asthma severity.<sup>21</sup>

Among women with asthma, we found no significant differences in the rates of preterm delivery less than 32 weeks or delivery less than 37 weeks (Table 3). Neither asthma nor asthma severity (moderate-severe or mild) was significantly related to preterm delivery by logistic regression analysis. There were no significant differences for antepartum, delivery or postpartum outcomes compared with controls except increased cesarean delivery rate among the moderate-severe group. Wheezing during labor was significantly associated with asthma severity. There were no significant differences in neonatal outcomes (Table 4), except for a discharge diagnosis of neonatal sepsis among the mild group compared with controls.



**Table 3.** Antepartum, Delivery, and Postpartum Outcomes

	Moderate-severe (n = 866)	Mild (n=873)	Control (n=881)	Overall P	Moderate-severe versus controls [Unadjusted OR (95% CI)]	Mild versus controls [Unadjusted OR (95% CI)]
Delivery < 32 weeks	26 (3.0)	30 (3.4)	29 (3.3)	.873	0.9 (0.5, 1.6)	1.0 (0.6, 1.8)
Delivery < 37 weeks	137 (15.8)	141 (16.1)	139 (15.8)	.973	1.0 (0.8, 1.3)	1.0 (0.8, 1.3)
Gestational diabetes	57 (6.6)	29 (3.3)	42 (4.8)	.007	1.4 (0.9, 2.1)	0.7 (0.4, 1.1)
Preeclampsia	107 (12.4)	106 (12.2)	98 (11.2)	.703	1.1 (0.8, 1.5)	1.1 (0.8, 1.5)
Preterm premature rupture of membranes	100 (11.6)	113 (13.0)	98 (11.2)	.484	1.0 (0.8, 1.4)	1.2 (0.9, 1.6)
Induced for fetal indication	21 (2.4)	23 (2.6)	15 (1.7)	.386	1.4 (0.7, 2.8)	1.6 (0.8, 3.0)
Chorioamnionitis	44 (5.1)	59 (6.8)	44 (5.0)	.197	1.0 (0.7, 1.6)	1.4 (0.9, 2.1)
Oligohydramnios	71 (8.2)	44 (5.1)	52 (5.9)	.021	1.4 (1.0, 2.1)	0.8 (0.6, 1.3)
Cesarean delivery	203 (23.4)	160 (18.3)	160 (18.2)	.007	1.4 (1.1, 1.7)*	1.0 (0.8, 1.3)
Cesarean delivery for fetal distress	35 (4.0)	35 (4.0)	35 (4.0)	.997	1.0 (0.6, 1.6)	1.0 (0.6, 1.6)
Wheezing during labor	195 (22.7)	116 (13.4)	3 (0.3)	<.001		
Gestational age at delivery (wk)	38.5 ± 3.1	38.3 ± 3.7	38.3 ± 3.6	.950		
Mean hours of labor	12.1 ± 9.2	12.9 ± 12.6	11.7 ± 9.4	.181		
Postpartum hemorrhage	60 (7.5)	63 (7.8)	44 (5.3)	.091	1.5 (1.0, 2.2)	1.5 (1.0, 2.2)

OR = odds ratio; CI = confidence interval.

Data presented as *N*(%) or mean ± standard deviation.

\* Logistic regression adjusted OR = 1.4 (95% CI 1.1, 1.8).

Based on univariate analysis indicating significance, we performed a post hoc logistic regression analysis for gestational diabetes, oligohydramnios, and cesarean delivery with severe asthma considered as a separate category (Table 5). We also included preterm delivery and small for gestational age because they have been increased among women who received oral corticosteroids treatment of asthma during pregnancy.<sup>8,16</sup> Gestational

diabetes and delivery at less than 37 weeks of gestation remained significantly increased compared to controls by adjusted odds ratio.

## DISCUSSION

Asthma was not associated with an increase in preterm delivery at less than 32 weeks of gestation. We chose

**Table 4.** Neonatal Outcomes

	Moderate-severe	Mild	Control	Overall P	Moderate-severe versus controls [unadjusted OR (95% CI)]	Mild versus controls [unadjusted OR (95% CI)]
Birth weight (g)	3146 ± 667	3116 ± 699	3160 ± 706	0.291		
Small for gestational age	60 (7.1)	59 (6.9)	51 (5.9)	0.579	1.2 (0.8, 1.8)	1.2 (0.8, 1.7)
Perinatal mortality	4 (0.5)	3 (0.3)	4 (0.5)	0.935	1.0 (0.2, 4.1)	0.7 (0.2, 3.4)
Hyaline membrane disease	18 (2.1)	21 (2.5)	13 (1.5)	0.365	1.4 (0.7, 2.9)	1.6 (0.8, 3.3)
Bronchopulmonary disease	8 (0.9)	6 (0.7)	2 (0.2)	0.165	4.1 (0.9, 19.3)	3.0 (0.6, 15.1)
Discharge diagnosis of neonatal sepsis	14 (1.7)	20 (2.3)	7 (0.8)	0.048	2.0 (0.8, 5.1)	2.9 (1.2, 7.0)*
Congenital anomaly	36 (4.2)	33 (3.9)	34 (3.9)	0.919	1.1 (0.7, 1.7)	1.0 (0.6, 1.6)
Patent ductus arteriosus	7 (0.8)	6 (0.7)	3 (0.4)	0.429	2.4 (0.6, 9.2)	2.0 (0.5, 8.1)
Neonatal intensive care unit admission	147 (17.3)	152 (17.8)	133 (15.4)	0.379	1.1 (0.9, 1.5)	1.2 (0.9, 1.5)
Intraventricular hemorrhage	1 (0.1)	7 (0.9)	4 (0.5)	0.099	0.2 (0.0, 2.3)	1.8 (0.5, 6.1)
Necrotizing enterocolitis	3 (0.3)	4 (0.5)	3 (0.3)	0.928	1.0 (0.2, 5.0)	1.3 (0.3, 6.0)
Transient tachypnea of newborn	34 (4.0)	37 (4.3)	35 (4.0)	0.934	1.0 (0.6, 1.6)	1.1 (0.7, 1.7)

OR = odds ratio; CI = confidence interval.

Data presented as *N*(%) or mean ± standard deviation.

\* Logistic regression adjusted OR = 2.9 (95% CI 1.2, 6.8).



**Table 5.** Logistic Regression Analysis for Severe Asthma Cohort Compared With Controls (*N* = 52)

	Severe asthma [ <i>N</i> (%)]	Unadjusted odds ratios (95% CI)	Adjusted odds ratios (95% CI)
Gestational diabetes	8 (15.4)	3.6 (1.6, 8.2)	3.0 (1.2, 7.8)
Oligohydramnios	6 (11.5)	2.1 (0.8, 5.1)	2.1 (0.9, 5.3)
Cesarean delivery	14 (26.9)	1.7 (0.9, 3.1)	1.6 (0.8, 3.1)
Delivery < 32 weeks	3 (5.8)	1.8 (0.5, 6.1)	1.6 (0.5, 5.5)
Delivery < 37 weeks	16 (30.8)	2.4 (1.3, 4.4)	2.2 (1.2, 4.2)
Small for gestational age	5 (9.8)	1.7 (0.7, 4.5)	1.6 (0.6, 4.4)
Discharge diagnosis of neonatal sepsis	2 (3.9)	5.0 (1.0, 24.7)	4.6 (0.9, 22.8)

CI = confidence interval.

Adjusted odds ratio covariates: previous preterm delivery, smoking status, African American versus other. Body mass index was also included in the model for gestational diabetes.

severe prematurity as our primary outcome for several reasons. The association of prematurity and asthma is biologically plausible; both are characterized by chronic processes that are mediated in part by increased inflammatory cytokines and increased smooth muscle reactivity. Preterm delivery at less than 32 weeks of gestation is clinically important, accounts for most of the perinatal morbidity and mortality due to prematurity,<sup>19</sup> and was reported to be increased among asthmatics receiving regular medications.<sup>8</sup> There have been inconsistent findings of an increased risk of prematurity among women with asthma.<sup>3–16</sup> We found an increased frequency of delivery at less than 37 weeks of gestation limited to the subset (*n* = 52) with severe asthma. This finding should be interpreted with caution; we could not control for the potential confounding effects of oral corticosteroid use because we used the need for oral corticosteroids as part of our definition to classify severe asthma. A large retrospective database study of 36,985 asthmatic patients did find an increased incidence of preterm births less than 37 weeks; the incidence of preterm births at less than 32 weeks was not reported.<sup>9</sup> The largest prospective studies have not found a significant association of preterm birth and asthma.<sup>10,14</sup>

Other than increased frequencies of cesarean delivery among patients with moderate-severe asthma, discharge diagnosis of neonatal sepsis among those with mild asthma, and gestational diabetes and delivery less than 37 weeks among the subset with severe asthma, we did not find increased perinatal or obstetrical morbidity compared with controls. Because a discharge diagnosis of neonatal sepsis was found only among the cohort with mild asthma, the clinical importance of this outcome is not clear; this finding may be related to type 1 error. Our findings are generally reassuring, despite a relatively high prevalence of asthma morbidity. After enrollment, 27.3% of women in the moderate-severe cohort had asthma exacerbations, and 8% of these required hospitalization.<sup>21</sup>

A potential explanation for the inconsistencies among previous studies regarding the effect of asthma on obstetrical and neonatal outcomes may include the fact that most studies of asthma during pregnancy did not attempt to classify asthma severity. Classification of asthma severity has important clinical implications with respect to asthma morbidity and tailoring optimal treatment regimens.<sup>1,20</sup> Failure to classify severity may result in suboptimal asthma control, thereby increasing risks for adverse maternal or neonatal outcomes. Oral corticosteroid treatment per se may confound maternal and neonatal outcomes. Some positive findings of our study and previous studies may be due to chance. In general, larger prospective studies have tended to find fewer significant adverse associations.<sup>10,14</sup> Our study has the strengths of being large, multicentered, prospective, stratified by asthma severity; including high-quality spirometry; and controlling for confounders, such as African-American ethnicity and smoking status.

The prospective nature of this study may have led to better surveillance and treatment. The low prevalence of adverse obstetrical and perinatal outcomes may have in part been the result of dissemination of the 1993 National Asthma Education Program guidelines for treating asthma during pregnancy. These include 4 integral components of asthma management, including using objective measures of pulmonary function, mitigating asthma triggers, patient education, and pharmacological management tailored for asthma severity with anti-inflammatory therapy for moderate or severe asthma.<sup>20</sup> This was an observational study in which our investigators were not mandated to follow National Asthma Education Program guidelines. However, they were familiar with the guidelines, and this study was conducted in parallel with a prospective randomized clinical trial in which all patients were managed using these guidelines. Aspects of asthma management, including medications, pulmonary function, compliance, and other outcomes, will be reported in future articles.



In 1997, the National Asthma Education Program published the Expert Panel Report II, in which the definitions of asthma severity were modified to include mild persistent asthma; however, these recommendations were not specific to pregnancy.<sup>1</sup> Based on the new classification, our moderate cohort would include subjects with both mild persistent and moderate persistent asthma.

Our study has several important limitations. Because this was an observational study, the management of asthma was not standardized. The diagnosis of asthma was attained primarily by eliciting a history of physician-diagnosed asthma, although this has been found to be a valid definition in epidemiological studies.<sup>24</sup> Control participants were not rigorously evaluated for absence of asthma. We did not take into account possible changes in asthma severity before enrollment in the study. Our enrolled population was heavily weighted toward single mothers and enriched for African Americans and those with subsidized insurance. This likely reflects the urban centers that make up the Maternal-Fetal Medicine Units network. However, because asthma is more common and more severe in African Americans<sup>2</sup> and more severe in patients with lower socioeconomic status,<sup>25,26</sup> this is an important population to study. This study controlled for confounding factors, such as ethnicity and type of insurance, and had a large sample size and wide geographic representation; these strengths should increase the generalizability of our reassuring findings to other populations. However, one should be cautious about inferring the generalizability of our results in our participants with severe asthma because of the relatively small size of this cohort in our study.

In conclusion, we had excellent maternal and perinatal outcomes despite a high frequency of asthma exacerbations. These findings do not contradict the possibility that suboptimal control of asthma during pregnancy is associated with increased risk to the mother or baby.

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