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# Obstetric complications among US women with asthma

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## Abstract

**Objective—**To characterize complications of pregnancy, labor and delivery associated with maternal asthma in a contemporary US cohort.

**Study Design—**A retrospective cohort based on electronic medical record data from 223,512 singleton deliveries from 12 clinical centers across the United States between 2002–2008.

**Results—**Women with asthma had higher odds of preeclampsia (adjusted odds ratio (aOR)=1.14; 95% confidence interval (95%CI)=1.06–1.22), superimposed preeclampsia (aOR=1.34; 95%CI=1.15–1.56), gestational diabetes (aOR=1.11; 95%CI=1.03–1.19), placental abruption (aOR=1.22; 95%CI=1.09–1.36), and placenta previa (aOR=1.30; 95%CI=1.08–1.56). Asthmatic women had a higher odds of preterm birth overall (aOR=1.17; 95%CI=1.12–1.23) and of medically-indicated preterm delivery (aOR=1.14; 95%CI=1.01–1.29). Asthmatics were less likely to have spontaneous labor (aOR=0.87; 95%CI=0.84–0.90) and vaginal delivery (aOR=0.84; 95%CI=0.80–0.87). Risks were higher for breech presentation (aOR=1.13; 95%CI=1.05–1.22), hemorrhage (aOR=1.09; 95%CI=1.03–1.16), pulmonary embolism (aOR=1.71; 95%CI=1.05–2.79), and maternal ICU admission (aOR=1.34; 95%CI=1.04–1.72).



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**Conclusion—**Maternal asthma increased risk for nearly all outcomes studied in a general obstetric population.

### Keywords

asthma; cesarean delivery; pregnancy complication; preterm birth

## Introduction

Asthma is the most common chronic disease in pregnancy, complicating 4–8% of pregnancies nearly 10 years ago[1] and the rate of asthma continues to increase. Approximately 10% of US women of reproductive age had active asthma in 2008–2010[2] and 4.2% used a bronchodilator medication at least once during the past month during 2005–2008[3]. In the National Hospital Discharge Survey, the rate of asthma reported during labor and delivery nearly doubled between 1993–1997 and 2001–2005[4].

A recent meta-analysis[5] concluded that maternal asthma increased the risk of low-birth weight and small for gestational age infants, preterm delivery and preeclampsia. Other conditions, such as gestational diabetes and serious obstetric complications (e.g., hemorrhage, plactental abruption, and placenta previa) are not consistently associated with maternal asthma, possibly due to underlying differences in patient populations, methodologic inadequacies (particularly for early studies), and relatively small numbers of women with asthma studied[6]. Studies generally find that outcomes are more adverse when asthma is poorly controlled[7] or when asthma is more severe [8;9], but few studies are large enough to examine specific risks for less common complications of pregnancy, labor and delivery. The objectives of this study were to use a large, recent cohort of women in the US to examine specific risks for complications of pregnancy, labor and delivery including less frequent adverse outcomes and to explore the reasons for the increased risk of preterm delivery in women with asthma.

## Materials and Methods

The Consortium on Safe Labor (CSL) included 12 clinical centers (with 19 hospitals) across 9 American College of Obstetricians and Gynecologists US districts. Details of the study and data collection procedures are described elsewhere[10]. Briefly, centers provided electronic medical records and discharge International Classification of Diseases, 9$^{th}$ revision (ICD-9) codes from the intrapartum admission for 228,562 pregnancies among 208,695 women between 2002–2008. The majority of the cohort (87%) delivered between 2005–2007. This analysis is restricted to singleton pregnancies (n=223,512) among 204,180 women. Most women (n=185,785; 83.1%) contributed only one pregnancy. Institutional review board approval was obtained by all participating institutions.

Most complications of pregnancy, labor and delivery as well as the diagnosis of asthma were derived from medical record data supplemented with ICD-9 codes where available (Supplemental Table 1). The source of case ascertainment (medical record or ICD-9 codes) varied by site. Overall, only 10.7% of asthma cases were reported in discharge ICD-9 codes alone while the remaining cases were noted in the medical record or both sources. We examined various obstetric outcomes including gestational hypertension, preeclampsia, superimposed preeclampsia, maternal seizure (with or without mention of hypertension), gestational diabetes, chorioamnionitis, placenta previa, placental abruption, hemorrhage, pulmonary embolism, postpartum fever, premature rupture of membranes (PROM), preterm PROM (PPROM, defined as PROM <37 gestational weeks), and breech presentation.

Outcomes derived solely from medical records include pre-labor cesarean delivery (defined as a cesarean delivery without any indication of labor and less than two vaginal exams after admission to hospital), induction, spontaneous labor, route of delivery (vaginal or cesarean), preterm birth (<37 gestational weeks), low birth weight (birth weight <2,500 g), intrauterine fetal death, maternal intensive care unit (ICU) admission and maternal death.

Pregnancy was the unit of analysis for all statistical testing. Descriptive statistics were calculated for all study variables and significance testing was based on either linear or logistic regression using generalized estimating equations (GEE) to account for correlations between pregnancies contributed by the same woman. Odds ratios and 95% confidence limits were calculated using logistic regression with GEE using a first order autoregressive covariance structure. Pregnancies among women without asthma were the reference group in all analyses. All reported odds are adjusted for site and fully adjusted models included site, maternal age, race/ethnicity, marital status, pre-pregnancy body mass index (BMI, weight in kg/height in meters squared), insurance status, smoking and alcohol use during pregnancy, presence of chronic disease (pre-existing diabetes, chronic hypertension, thyroid disease, or HIV) and parity. Women with chronic hypertension were excluded from the analyses of gestational hypertension and preeclampsia. Women with pre-existing diabetes were excluded from the analyses of gestational diabetes. In the analyses of superimposed preeclampsia, women with chronic hypertension were not categorized as having a chronic disease unless they had another chronic condition. Analyses regarding labor and route of delivery were also adjusted for prior cesarean delivery.

Multiple sensitivity analyses were conducted, first to test the robustness of our findings given potential bias or error in medical record ascertainment, including restriction to women with ICD-9 coded asthma as these women may be more likely to have active asthma (as opposed to a past history); removing sites with asthma rates at the tails of the distribution (two sites each at the high and the low end), restriction to sites with complete data and finally, restriction to patients with no missing data. Results from these logistic regression with GEE analyses yielded similar findings, so only the full sample analysis is presented. We also ran two subgroup analyses: 1)restricted to nulliparas to explore the potential for residual confounding by past history of preterm delivery, cesarean delivery or other prior complications in multiparas and 2) restricted to preterm deliveries to determine if the precursors of preterm delivery were different for women with asthma.

All statistical analyses were performed using PROC GENMOD in SAS software (version 9.2, SAS Institute Inc., North Carolina, US).

## Results

Maternal asthma complicated 7.6% of singleton pregnancies. Mothers with asthma were younger (26.2 years vs. 27.5 years; $p<0.0001$) and more likely to be non-Hispanic Black, unmarried, and have public insurance than their counterparts without asthma (Table 1). Women with asthma were more likely to be obese prior to pregnancy and also more likely to have smoking (12.2% vs. 6.2%; $p<0.0001$) or alcohol use (3.1% vs. 1.7%; $p<0.0001$) during pregnancy recorded in their medical records. Pregnancies complicated by asthma had a significantly greater burden of other chronic diseases as well (8.2% vs. 6.2%, $p<0.0001$). Parity was similar among pregnancies with and without asthma but among multiparas, women with asthma had more prior cesarean deliveries (15.3% vs. 14.0%; $p<0.0001$).

Analyses of the complications of pregnancy, labor and delivery encountered by women with and without asthma (Table 2) demonstrate a general pattern of increased risk for asthmatic pregnancies.

### Hypertensive disorders of pregnancy and maternal seizure

Fully adjusted models indicate increased odds of superimposed preeclampsia (adjusted odds ratio (aOR)=1.34; 95% confidence interval (95%CI)=1.15–1.56) and preeclampsia, (aOR=1.14, 95%CI=1.06–1.22). Eclampsia was significantly associated with maternal asthma in site-adjusted models (OR=1.61, 95%CI=1.10–2.36) but the risk was attenuated after full adjustment (aOR=1.41, 95%CI=0.96–2.07). After observing a significant relationship between asthma and maternal seizure, we stratified seizures by hypertension status and found the increased risk of maternal seizure was primarily in the hypertensive group (aOR=2.37, 95%CI=1.40–4.02), suggesting that eclampsia may not have been fully captured in our dataset. Gestational hypertension was elevated in site-adjusted models but not significant after further adjustment.

### Other pregnancy complications

Gestational diabetes (aOR=1.11, 95%CI=1.03–1.19) and placenta previa (aOR=1.30, 95%CI=1.08–1.56) were both increased, but chorioamnionitis was similar in pregnancies with and without asthma.

### Complications of labor and delivery

Asthmatic pregnancies had an increased likelihood of being scheduled for pre-labor cesarean delivery (aOR=1.16, 95%CI=1.09–1.23) or of being induced (aOR=1.10, 95%CI=1.06–1.14) compared to pregnancies without asthma. Asthmatic women were more likely to have a cesarean delivery than women without asthma regardless of whether they present in spontaneous labor (10.3 vs. 9.1%; p=0.0003) or undergo labor induction (8.1% vs.7.1%; p<0.0001). As a result, pregnancies with maternal asthma had a lower odds overall of vaginal delivery (aOR=0.84, 95%CI=0.80–0.87).

Premature rupture of membranes (PROM) was similar in pregnancies with and without asthma (7.1% versus 7.0%; p=0.98) but preterm PROM was higher in asthmatics (3.0% versus 2.2%; p<0.0001). Fetal presentation also varied by asthma status with more breech presentations among pregnancies complicated by asthma (aOR=1.13, 95%CI=1.05–1.22).

With regard to severe complications, the odds of placental abruption (aOR=1.22, 95%CI=1.09–1.36), hemorrhage (aOR=1.09, 95%CI=1.03–1.16), pulmonary embolism (aOR=1.71, 95%CI=1.05–2.79) and maternal ICU admission (aOR=1.34, 95%CI=1.04–1.72) were all significantly increased in pregnancies with asthma but there was no difference in postpartum fever and maternal death.

As anticipated, both low birth weight (aOR=1.16, 95%CI=1.10–1.23) and preterm delivery (aOR=1.17, 95%CI=1.12–1.23) were increased in pregnancies with asthma but the odds of intrauterine fetal death were not significantly higher compared to pregnancies without asthma. Restricting these analyses to nulliparas yielded similar findings (data not shown).

With respect to preterm delivery (Table 3), we found no significant differences in prelabor cesarean deliveries (aOR=1.06, 95%CI=0.95–1.19), spontaneous labor (aOR=0.93, 95%CI=0.85–1.01), or induction (aOR=1.04, 95%CI=0.94–1.15) and women with asthma were no more likely than those without to have a cesarean delivery. However, further examination of the precursors of preterm delivery demonstrated that women with asthma had more medically-indicated preterm deliveries (aOR=1.14, 95%CI=1.01–1.29) and were less likely to deliver preterm after a spontaneous process (labor or PPROM) (aOR=0.89, 95%CI=0.81–0.97).

## Comment

Women with asthma begin pregnancy with a more unfavorable profile of demographic, lifestyle and clinical risk factors including increased obesity, smoking and a higher burden of other chronic diseases. Even after adjustment for these and other risk factors, asthma was independently associated with higher odds for nearly all complications of pregnancy, labor and delivery under study. Notably, asthmatic women experienced more serious complications including preeclampsia, preterm birth, cesarean delivery, placenta previa, placental abruption, hemorrhage, and pulmonary embolism, with a 34% increased odds of ICU admission. Neonates born to women with asthma were also more likely to be low birth weight.

Our findings are consistent with the recent review and meta-analysis by Murphy and colleagues[5] that concluded risks were increased for preeclampsia, low birth weight and preterm delivery in women with asthma. The literature on other complications of pregnancy is less consistent, although several studies reviewed by Dombroski[6] have reported increased risk for cesarean delivery and maternal hemorrhage.

An observational cohort conducted by the Maternal-Fetal Medicine Units (MFMU) network found increased risk for cesarean delivery but only observed increased risks for gestational diabetes and preterm delivery in women with severe asthma (but the number of cases with severe asthma were small: 8 for GDM and 16 for preterm delivery)[8]. In contrast, in our fully adjusted models which have substantially more cases with asthma (927 with GDM and 2526 preterm pregnancies) but no information on severity, we observed an 11% increase in the odds of gestational diabetes and 17% increase in preterm birth compared to pregnancies without asthma.

Results from prior large retrospective cohorts that examined obstetric complications have also provided conflicting results. Increased risk of miscarriage, hemorrhage, cesarean delivery and anemia were reported in UK primary care health system records for pregnancies with asthma from 1988–2004[11] but risk for placental abruption, placenta previa, hypertensive disorders, diabetes, and other chronic disease with the exception of depression were not elevated. Approximately 35 percent of women in the study contributed more than one pregnancy but the statistical modeling did not control for correlation between pregnancies to the same women and the rates of complications observed were generally lower than our findings. In contrast, a Medicaid-based study in Tennessee covering births from 1995–2003 observed higher risk for hypertensive disorders, hemorrhage, gestational diabetes, cesarean section and low birth weight but not for preterm delivery[7]. Again, it was unclear how the authors controlled for multiple deliveries to the same women. Failing to control for the correlated pregnancies within women would likely overestimate the risks observed in these populations, but curiously, this was one of the few studies not to report a risk for preterm delivery[5].

To our knowledge, no prior studies have examined risk for pulmonary embolism in relation to maternal asthma. Pulmonary embolism remains a leading cause of maternal mortality[12] and we observed twice as many cases in pregnancies complicated by asthma compared to those without asthma (12/10,000 vs. 6/10,000 deliveries, respectively). It may be that this risk was secondary to the higher rate of cesarean delivery or thrombosis associated with preeclampsia but since the number of cases in our study was relatively small (n=20 among women with asthma), the cause remains unknown. As embolism represents another vascular endpoint with serious consequences found to be associated with asthma, further research is needed to confirm this novel finding.

Asthma is a complex chronic disease and the underlying immune dysfunction may increase the likelihood of poor placentation, resulting in both increases in gestational hypertensive disorders and placenta previa or abruption. Mothers with asthma have high risk profiles, so their low likelihood of spontaneous labor (with more induction and pre-labor cesarean section) may be expected but even when women with asthma labored, they were significantly less likely to have a vaginal delivery than their non-asthmatic counterparts. Perhaps the increased risk of pregnancy complications observed with asthma (e.g. preeclampsia) also contributed to unsuccessful attempted vaginal delivery. Physician-diagnosed asthma increased risk for idiopathic preterm labor in a small case-control study from Quebec[13] but the authors did not observe effects associated with methacholine challenge suggesting nonatopic, noncholinergic mechanisms. Our data suggest an increased risk of eclampsia, significant in a site-adjusted model, and given the high risk for maternal seizure when hypertensive disorders were noted in the medical record, cases of eclampsia likely were miscoded. This assumption is supported by the fact that very few women had epilepsy or other seizure disorders, so our finding that risk of maternal seizure or eclampsia is increased in women with asthma may be another indication of the confluence of factors leading from poor immunologic adaptation to pregnancy to preeclampsia/eclampsia[14].

The strengths of this analysis include having clinical data from a large, contemporary US population. The number of women with asthma in the obstetric population continues to increase and as management of asthma continues to improve[15;16], more recent data are valuable to examine the impact of maternal asthma on obstetric outcomes. The electronic medical records and discharge summaries provide a wealth of rich clinical data and the large sample size allows for rigorous analysis of less common, but more serious obstetric complications. With over 17,000 pregnancies with asthma, we have one of the largest study populations to date. We are, however, limited by the data captured in the intrapartum records and discharge summaries. Not all clinical centers provided comparable data, but an intensive chart review of key variables compared to the electronic records found very good agreement[10] and we conducted a series of sensitivity analyses to test the robustness of our findings (restricted to sites with lower variability in asthma prevalence, to sites with complete data, patients with complete data, and only pregnancies with ICD-9 confirmed asthma) and found similar results.

The major limitation of our study is the lack of information on asthma control, exacerbations, and treatment. Several studies have shown that adverse outcomes are more common (or only occur) in pregnancies with poor asthma control[7;9;17]. Presumably, the asthma cases in our study represent a mix of severity and treatment and we cannot evaluate how well our findings apply to the subgroup of women with well controlled asthma. It is possible that records could be biased and more likely to include the diagnosis of asthma when complications arise, but the overall prevalence of asthma we observed (7.6%) was similar to the general population estimates of 10% for women of reproductive age and of asthma in pregnancy reported in the early 2000's (4%–8%)[1].

Our findings confirm that women with asthma have an increased risk of preeclampsia, preterm birth and low birth weight[5]. Since chronic inflammation is a hallmark of asthma and increases in pro-inflammatory cytokines play an important role in triggering the spontaneous onset of labor,[18] we considered the potential pathways leading to preterm delivery. However, when we examined the precursors of preterm delivery in our data, medically-indicated delivery was more common in asthmatic pregnancies and women with asthma were less likely to deliver as a result of a spontaneous process (labor or PPROM). This suggests that the increased risk of preterm birth among women with asthma is not driven by spontaneous preterm labor but rather is due to their compromised medical condition.

Inflammation related to asthma does not seem to be triggering preterm labor at the population level.

We also found that asthma increased the risk of other serious obstetric complications including placental abruption, hemorrhage, pulmonary embolism and maternal ICU admission as well as increasing risk for gestational diabetes, breech presentation and cesarean delivery. The National Asthma Education and Prevention Program and ACOG have published guidelines for evaluation and treatment for asthma in pregnancy[15;16] and clinical strategies to manage women with asthma and improve outcomes have been well-described[19]. Monitoring peak flow as an estimate of forced expiratory volume in one second ($FEV_1$) is recommended and good control of asthma symptoms has been associated with improved outcomes, particularly for preterm birth. For example, more than 21% of women with poor spirometry across pregnancy ($FEV_1$ <80% of expected) delivered preterm in the MFMU network study, compared to 15% when FEV1 was more favorable (≥80% of expected)[9]. Asthma should be actively managed during pregnancy including objective assessment of symptoms and lung function, avoidance of asthma triggers, patient education and step therapy to adjust the number and frequency of medications needed to control symptoms[19]. The importance of good asthma control for the wellbeing of the baby should be clearly communicated to the patient, particularly for those who may resist taking needed medication due to concern about the impact of pharmaceuticals on the fetus.

Given that asthma is the most common chronic condition in pregnancy and the proportion of women of reproductive age with asthma is likely to increase for the foreseeable future, our findings are concerning. We observed a pattern of increased risk for nearly all outcomes studied in the general obstetric population which likely included women with mild asthma and good asthma control. Since both asthma severity and control contribute to morbidity during pregnancy, more research is needed to determine factors that predict poor obstetric outcomes and determine if certain vulnerable women can benefit from targeted intervention to ameliorate their obstetric risks. Our data from a large, contemporary, nationwide US cohort suggest that we still have a long way to go to improve obstetric outcomes for women with asthma.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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A portion of these findings were presented at the 23rd annual meeting of the International Society for Environmental Epidemiology, Barcelona, Spain, September 13–16, 2011 and an updated analysis will be presented at the 2012 annual meeting of the American College of Epidemiology, Chicago, IL, September 8–11, 2012.

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### Clinical Implications

- Asthma significantly increased risk for nearly every obstetric complication studied including more serious complications such as preeclampsia, preterm birth, cesarean delivery, placenta previa, placental abruption, hemorrhage, and pulmonary embolism, along with a 34% increased odds of ICU admission.
- Women with asthma generally have an unfavorable risk profile when they enter pregnancy compared to non-asthmatics, with a higher prevalence of obesity, smoking, and other chronic diseases, but their higher rates of obstetric complications were not explained by demographic or clinical risk factors.
- Preterm delivery among asthmatics was more likely to be medically indicated and not the result of a spontaneous process (labor or PROM).
- The increased risk for adverse outcomes due to asthma on the population level in the US indicates that more work needs to be done to ameliorate the impact of maternal asthma.

## Table 1

Maternal demographic, lifestyle and clinical characteristics among singleton pregnancies with and without maternal asthma (n=223,512), Consortium on Safe Labor, 2002–2008.

| Maternal characteristics | No Asthma n=206,468 Frequency (%)/Mean (sd) | Asthma n=17,044 Frequency (%)/Mean (sd) | Site-adjusted p-value[a] |
|---|---|---|---|
| **DEMOGRAPHIC FACTORS** | | | |
| **Maternal age (yrs)** | 27.5 (6.2) | 26.6 (6.2) | <0.0001 |
| **Race** | | | |
| Non-Hispanic White | 102447 (49.6) | 8156 (47.9) | <0.0001 |
| Non-Hispanic Black | 44840 (21.7) | 5444 (31.9) | |
| Hispanic | 36543 (17.7) | 2288 (13.4) | |
| Asian | 8970 (4.3) | 211 (1.2) | |
| Other | 4966 (2.4) | 265 (1.6) | |
| Missing | 8702 (4.2) | 680 (4.0) | |
| **Marital status** | | | |
| Not married | 76248 (36.9) | 8765 (51.4) | <0.0001 |
| Married | 123800 (60.0) | 7461 (43.8) | |
| Missing | 6420 (3.1) | 818 (4.8) | |
| **Insurance** | | | |
| Private | 116084 (56.2) | 8883 (52.1) | <0.0001 |
| Public | 65097 (31.5) | 7105 (41.7) | |
| Other | 2774 (1.3) | 208 (1.2) | |
| Missing | 22513 (10.9) | 848 (5.0) | |
| **Pregnancies per woman** | | | |
| 1 | 172355 (91.2) | 14074 (90.7) | |
| 2 | 15878 (8.4) | 1355 (8.7) | |
| 3 | 724 (0.4) | 80 (0.5) | |
| 4 | 45 (0.02) | 5 (0.03) | |
| 5 | 1 (<.01) | 0 (0.0) | |
| **CLINICAL FACTORS** | | | |
| **Pre-pregnancy BMI (kg/m$^2$)** | | | |
| Underweight (<18.5) | 7517 (3.6) | 463 (2.7) | <0.0001 |
| Normal weight (18.5–<25) | 74442 (36.1) | 4641 (27.2) | |
| Overweight (25–<30) | 30909 (15.0) | 2614 (15.3) | |
| Obese (30–<35) | 14212 (6.9) | 1530 (9.0) | |
| Severely obese (≥35) | 10553 (5.1) | 1605 (9.4) | |
| Unknown | 68835 (33.3) | 6191 (36.3) | |
| **Smoking during pregnancy** | 12858 (6.2) | 2075 (12.2) | <0.0001 |
| **Alcohol during pregnancy** | 3559 (1.7) | 532 (3.1) | <0.0001 |
| **Pre-existing diabetes** | 2931 (1.4) | 381 (2.2) | <0.0001 |

| Maternal characteristics | No Asthma n=206,468 Frequency (%)/Mean (sd) | Asthma n=17,044 Frequency (%)/Mean (sd) | Site-adjusted p-value[a] |
|---|---|---|---|
| **Chronic hypertension** | 3733 (1.8) | 480 (2.8) | <0.0001 |
| **Thyroid disease** | 6043 (2.9) | 568 (3.3) | 0.003 |
| **HIV/AIDS** | 778 (0.4) | 107 (0.6) | <0.0001 |
| **Any chronic disease (diabetes, hypertension, thyroid, HIV)** | 12722 (6.2) | 1404 (8.2) | <0.0001 |
| **Parity** | | | |
| Nulliparous | 82417 (39.9) | 6824 (40.0) | 0.84 |
| Multiparous | 124051 (60.1) | 10220 (60.0) | |
| **Prior C-section** | | | |
| Nullipara | 82417 (39.9) | 6824 (40.0) | <0.0001 |
| Multipara - No | 95123 (46.1) | 7608 (44.6) | |
| Multipara - Yes | 28928 (14.0) | 2612 (15.3) | |

[a] p-values are based on generalized estimating equations that account for multiple pregnancies to the same woman.

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**Table 2**

Complications of pregnancy, labor and delivery for singleton deliveries among US women with asthma, Consortium on Safe Labor, 2002–2008.

| Outcomes | No Asthma n=206,468 Frequency (%) | Asthma n=17,044 Frequency (%) | Site-Adjusted p-value[a] | Site-Adjusted Odds Ratio (95% CI)[a] | Fully-Adjusted Odds Ratio (95% CI)[b] |
|---|---|---|---|---|---|
| **Hypertensive disorders of pregnancy** | | | | | |
| Superimposed preeclampsia | 1680 (0.8) | 213 (1.3) | <0.0001 | 1.54 [1.33, 1.79] | 1.34 [1.15, 1.56] |
| Eclampsia | 207 (0.1) | 33 (0.2) | 0.01 | 1.61 [1.10, 2.36] | 1.41 [0.96, 2.07] |
| Preeclampsia | 9628 (4.7) | 924 (5.4) | <0.0001 | 1.24 [1.16, 1.33] | 1.14 [1.06, 1.22] |
| Gestational hypertension | 5523 (2.7) | 557 (3.3) | 0.0003 | 1.18 [1.08, 1.30] | 1.08 [0.98, 1.19] |
| **Maternal seizure** | | | | | |
| All maternal seizures | 176 (0.1) | 33 (0.2) | 0.0008 | 1.93 [1.32, 2.83] | 1.79 [1.21, 2.63] |
| Maternal seizure without hypertension noted | 93 (0.05) | 14 (0.09) | 0.19 | 1.45 [0.83, 2.55] | 1.35 [0.77, 2.37] |
| Maternal seizure with hypertension noted | 83 (0.05) | 19 (0.12) | 0.0006 | 2.51 [1.48, 4.25] | 2.37 [1.40, 4.02] |
| **Other pregnancy complications** | | | | | |
| Gestational diabetes | 10420 (5.1) | 927 (5.4) | 0.06 | 1.07 [1.00, 1.15] | 1.11 [1.03, 1.19] |
| Chorioamnionitis | 6415 (3.1) | 504 (3.0) | 0.32 | 1.05 [0.95, 1.16] | 1.06 [0.96, 1.17] |
| Placenta previa | 1444 (0.7) | 141 (0.8) | 0.06 | 1.19 [0.99, 1.42] | 1.30 [1.08, 1.56] |
| **Complications of labor and delivery** | | | | | |
| Prelabor cesarean delivery | 23688 (11.5) | 2193 (12.9) | <0.0001 | 1.15 [1.10, 1.21] | 1.16 [1.09, 1.23] |
| Spontaneous labor | 111523 (54.0) | 8921 (52.3) | <0.0001 | 0.86 [0.84, 0.89] | 0.87 [0.84, 0.90] |
| Cesarean delivery after spontaneous labor | 18835 (9.1) | 1749 (10.3) | 0.0003 | 1.10 [1.05, 1.16] | 1.06 [1.00, 1.12] |
| Induction | 71257 (34.5) | 5930 (34.8) | <0.0001 | 1.10 [1.06, 1.13] | 1.10 [1.06, 1.14] |
| Cesarean delivery after induction | 14746 (7.1) | 1381 (8.1) | <0.0001 | 1.22 [1.15, 1.29] | 1.17 [1.10, 1.24] |
| All vaginal delivery | 149199 (72.3) | 11721 (68.8) | <0.0001 | 0.84 [0.81, 0.87] | 0.84 [0.80, 0.87] |
| PPROM | 4596 (2.2) | 516 (3.0) | <0.0001 | 1.23 [1.12, 1.36] | 1.18 [1.07, 1.30] |
| PROM | 14379 (7.0) | 1212 (7.1) | 0.98 | 1.00 [0.94, 1.07] | 0.99 [0.93, 1.05] |
| Breech presentation | 8785 (4.3) | 811 (4.8) | 0.01 | 1.10 [1.02, 1.19] | 1.13 [1.05, 1.22] |
| Placental abruption | 3242 (1.6) | 380 (2.2) | <0.0001 | 1.27 [1.14, 1.42] | 1.22 [1.09, 1.36] |
| Maternal hemorrhage | 13423 (6.5) | 1292 (7.6) | 0.001 | 1.11 [1.04, 1.18] | 1.09 [1.03, 1.16] |
| Maternal pulmonary embolism | 114 (0.06) | 20 (0.12) | 0.008 | 1.90 [1.18, 3.07] | 1.71 [1.05, 2.79] |

| Outcomes | No Asthma n=206,468 Frequency (%) | Asthma n=17,044 Frequency (%) | Site-Adjusted p-value[a] | Site-Adjusted Odds Ratio (95% CI)[a] | Fully-Adjusted Odds Ratio (95% CI)[b] |
|---|---|---|---|---|---|
| Maternal postpartum fever | 5531 (2.7) | 532 (3.1) | 0.35 | 1.05 [0.95, 1.15] | 0.99 [0.90, 1.09] |
| Maternal ICU admission | 902 (0.6) | 73 (0.6) | 0.01 | 1.38 [1.08, 1.76] | 1.34 [1.04, 1.72] |
| Maternal death | 18 (0.01) | 1 (0.01) | 0.70 | Not calculated | Not calculated |
| Low birth weight (<2500 g) | 16551 (8.1) | 1815 (10.7) | <0.0001 | 1.26 [1.19, 1.33] | 1.16 [1.10, 1.23] |
| Preterm birth (<37 weeks) | 23618 (11.4) | 2526 (14.8) | <0.0001 | 1.25 [1.19, 1.31] | 1.17 [1.12, 1.23] |
| Intrauterine fetal death | 1148 (0.6) | 110 (0.7) | 0.26 | 1.12 [0.92, 1.38] | 1.07 [0.87, 1.32] |

Abbreviations: PPROM, preterm premature rupture of membranes; PROM, premature rupture of membranes; ICU, intensive care unit.

P-values are based on generalized estimating equations that account for multiple pregnancies to the same woman. All P-values are adjusted for site.

Women with and without asthma had following rates of missing data: 5.9% and 6.9% on vertex presentation, 24.0% and 21.3% on ICU admission, 8.5% and 11.0% on seizures, and 0.8% and 1.1% on birth weight.

[a]Adjusted for site.

[b]Adjusted for site; maternal age; maternal race; marital status; insurance; pre-pregnancy BMI; smoking during pregnancy; alcohol use during pregnancy; history of either pre-existing diabetes (except for gestational diabetes), HIV, chronic hypertension (except for gestational hypertension, preeclampsia, eclampsia or maternal seizure with hypertension), or thyroid disease; parity (spontaneous labor, induction, cesarean delivery, and vaginal delivery adjusted for prior cesarean delivery instead of parity alone).

**Table 3**

Labor and delivery characteristics and precursors for preterm (<37 weeks) singleton deliveries among US women with asthma, Consortium on Safe Labor, 2002–2008.

| | No Asthma n=23,618 Frequency (%) | Asthma n=2,526 Frequency (%) | Site-Adjusted p-value[a] | Site-Adjusted Odds Ratio (95% CI)[a] | Fully-Adjusted Odds Ratio (95% CI)[b] |
|---|---|---|---|---|---|
| **LABOR/DELIVERY CHARACTERISTICS** | | | | | |
| Prelabor cesarean delivery | 4625 (19.6) | 511 (20.2) | 0.22 | 1.07 [0.96, 1.19] | 1.06 [0.95, 1.19] |
| Spontaneous labor | 12726 (53.9) | 1345 (53.3) | 0.08 | 0.93 [0.85, 1.01] | 0.93 [0.85, 1.01] |
| Cesarean delivery after spontaneous labor | 3172 (13.4) | 359 (14.2) | 0.22 | 1.08 [0.96, 1.22] | 1.07 [0.94, 1.21] |
| Induction | 6267 (26.5) | 670 (26.5) | 0.42 | 1.04 [0.95, 1.15] | 1.04 [0.94, 1.15] |
| Cesarean delivery after induction | 1606 (6.8) | 176 (7.0) | 0.39 | 1.07 [0.91, 1.27] | 1.02 [0.86, 1.21] |
| **PRETERM PRECURSOR** | | | | | |
| PPROM | 4596 (19.5) | 516 (20.4) | 0.86 | 1.01 [0.91, 1.12] | 1.02 [0.92, 1.13] |
| Spontaneous process (labor or PPROM) | 15359 (65.0) | 1609 (63.7) | 0.009 | 0.89 [0.81, 0.97] | 0.89 [0.81, 0.97] |
| Indicated | 3297 (14.0) | 404 (16.0) | 0.06 | 1.13 [1.00, 1.27] | 1.14 [1.01, 1.29] |
| Elective or no recorded indication | 8824 (37.4) | 913 (36.1) | 0.98 | 1.00 [0.92, 1.09] | 1.00 [0.91, 1.09] |

Abbreviations: PPROM=preterm premature rupture of membranes.

[a] P-values are based on generalized estimating equations that account for multiple pregnancies to the same woman. All P-values are adjusted for site.

[b] Adjusted for site; maternal age; maternal race; marital status; insurance; pre-pregnancy BMI; smoking during pregnancy; alcohol use during pregnancy; history of either pre-existing diabetes, HIV, chronic hypertension, or thyroid disease; and parity/prior cesarean section.