

More Reason to Watch Your Weight During Pregnancy



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Asthma is one of the most common chronic medical problems to complicate pregnancy, and asthma may adversely affect both maternal quality of life and perinatal outcomes. Recent US National surveys report that the prevalence of asthma during pregnancy is approximately 8.8%.¹ Data from observational studies have shown a strong association between poor asthma control and adverse perinatal outcomes.

The prevalence of obesity in women of reproductive age is estimated to be around 20%.² Obesity during pregnancy has been associated with adverse perinatal outcomes including: gestational diabetes, preeclampsia, thromboembolic disorders, postpartum hemorrhage, large for gestational age, fetal death, and congenital anomalies. The mechanisms leading to these outcomes are thought to be due to a heightened inflammatory response. Adipose tissue macrophages, whose density is in direct proportion to the degree of obesity, can secrete inflammatory markers including IL-6, TNF, and CCL2, which can have downstream effects on the liver, muscles, and placenta.³

Asthma exacerbations during pregnancy have been shown to occur at a rate of up to 6% from a UK database study of 12,828 pregnant women with asthma.² Gestational asthma exacerbations have also been shown to have a significant effect on perinatal outcomes, including low birth weight and preterm delivery.⁴ Previously reported risk factors for gestational asthma exacerbations include worsening chronic asthma during pregnancy, smoking, nonadherence to medications, viral respiratory infections, and possibly fetal sex.⁵ Higher body mass index (BMI) has been associated with an increased risk for asthma exacerbations in the nonpregnant asthmatic population.⁶ Similarly, in one prior study of pregnant asthmatic women, 30.7% were obese (BMI ≥ 30 kg/m²) compared with controls, and obesity was associated with an increase in asthma exacerbations (odds ratio [OR] 1.3, 95% confidence interval [CI] 1.1-1.7) compared with nonobese asthmatic women.⁷ The mechanisms thought to be responsible for the observed increased risk of asthma exacerbations related to obesity have included vitamin D deficiency, viral infections, and decreased corticosteroid responsiveness. Vitamin D levels decrease and respiratory viral infections increase in fall and winter, and in a cohort of 17,316 adult asthmatics, higher BMI values increased the risk for asthma exacerbations during these seasons.⁸

Not until this issue's article from Murphy et al⁹ has there been a study that attempts to describe the nature of inflammation driving asthma exacerbations in obese and overweight pregnant asthmatics. This report was a secondary analysis of a prospective study of respiratory viral-induced exacerbations during pregnancy. At the same time, some women also participated in a randomized control trial, The Managing Asthma in Pregnancy Study, in which women had their asthma treatment adjusted based on symptoms, lung function, and fractional exhaled nitric oxide (FeNO). BMI was obtained in early pregnancy as well as gestational weight gain, calculated from the second and third trimesters. The authors found that exacerbations occurred more in overweight (51.1%) and obese groups (48.4%) compared with the healthy weight group (25%, $P = .026$). In addition, oral corticosteroid use and higher weekly doses of inhaled corticosteroids were more frequently seen in the obese and overweight groups. The authors also obtained peripheral blood levels of IL-6, CRP, and sCD-163, a marker of macrophage activation. These biomarkers were higher in overweight and obese subjects, but only levels of CD-163 were significantly associated with an increased risk of asthma exacerbations.

One of the strengths of this study is in its prospective design of actively treated pregnant asthmatics and the inclusion of asthmatics with excessive weight gain during pregnancy. It is reassuring that excessive weight gain was not associated with exacerbations, systemic inflammation, or adverse perinatal outcomes. This study also provided information on asthma control as measured by the Asthma Control Questionnaire (ACQ) and severity. There appeared to be no differences between groups in regard to ACQ scores or frequency of short-acting β -agonist use. Therefore, the increased risk of exacerbations in overweight and obese women did not appear to be due to increased asthma severity or lack of asthma control.

The authors observed that a higher proportion of overweight and obese women experienced gestational hypertension and gestational diabetes. Hendler et al⁷ also reported an increased risk of preeclampsia or gestational hypertension (OR 1.7) and gestational diabetes (OR 4.2), as well as an increased risk of caesarean section (OR 1.6), in obese pregnant asthmatic women, but multivariable analysis in asthmatic and control women suggested that this increased risk was related to obesity, not asthma. Reassuring data from a large Canadian cohort of pregnant asthmatics found that obese asthmatic women were not at a higher risk of giving birth to small for gestational age infants (OR 0.6, 95% CI 0.4-1.1), large for gestational age infants (OR 1.2, 95% CI 0.7-2.2), or preterm delivery (OR 0.7, 95% CI 0.4-1.3).¹⁰

Limitations of the study by Murphy et al⁹ include not having a large enough sample to be able to adjust for potential confounding variables and not including a cohort of nonasthmatic obese pregnant women to further evaluate effects on perinatal outcomes. By including a nonasthmatic control group and

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adjusting for important confounders, Hendler et al⁷ were able to determine that the increased prevalence of gestational hypertension and gestational diabetes was the effect of obesity, rather than asthma. However, potential confounders for the increased risk of asthma exacerbations observed in obese and overweight women in the current study, such as maternal age, smoking, ethnicity, and education, were balanced between groups.

In the era of personalized medicine, it would be ideal to identify a clinically usable biomarker that might identify asthmatic pregnant women with an elevated risk of complications. Peripheral blood hyaluronic acid, soluble urokinase plasminogen activator receptor, and circulating periostin levels have not been shown to be useful biomarkers during pregnancy.¹¹⁻¹³ FeNO has been used to guide asthma management during pregnancy, and a management algorithm that included FeNO reduced the rate of asthma exacerbations.¹⁴ In the present study, the authors chose to measure the biomarkers sCD-163, CRP, and IL-6. From the data provided by Murphy et al,⁹ sCD-163 deserves a second look as to its utility as a possible tool clinicians may use in the management of pregnant asthmatic patients. This study also reinforces the need for women to avoid being overweight during pregnancy as an additional way to reduce their risk of asthma exacerbations, which can have adverse effects on both the mother and the infant.

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