

Asthma in Pregnancy: Diagnosis and Management

Asthma is a common, potentially serious, even life-threatening, chronic medical condition seen amongst nearly all groups of patients, regardless of ethnicity and socioeconomic circumstances. This article addresses the group of pregnant women with symptomatic asthma as well as those whose asthma is asymptomatic as a result of good control. The classification of these patients and appropriate management strategies are discussed.

Overall, the prevalence and morbidity of asthma are increasing; although mortality rates have decreased.¹ Asthma complicates 3.7% to 8.4% of all pregnancies—between 200,000 and 376,000 pregnancies annually in the United States.²⁻⁴ Acute exacerbations that necessitate emergency care or hospitalization have been reported in 9% to 11% of pregnant women cared for by asthma specialists. Most women with asthma have an uneventful pregnancy course; however, some may experience life-threatening exacerbations requiring hospitalization, intubation, intensive care management, and, rarely, preterm delivery.⁵

Treatment varies, based on the severity classification of each individual patient's asthma and includes avoidance of triggers, medications, and close monitoring. The ultimate goal of therapy is to reduce the number of hypoxemic episodes (ie, acute exacerbations and chronic symptoms) in the mother.

PATHOPHYSIOLOGY OF ASTHMA

Asthma is characterized by paroxysmal or persistent symptoms of broncho-constriction including breathlessness, chest tightness, cough, and sputum production. Diagnosis requires improvement in symptoms as well as objective changes in pulmonary function tests such as FEV1 or PEFr with administration of a beta-agonist. Diagnosis of asthma in pregnancy is no different from that in the non-pregnant patient.

The most common cause of respiratory symptoms such as shortness of breath in pregnancy is physiologic dyspnea of pregnancy and not asthma or other pathology. However, dyspnea of pregnancy does not typically have the associated cough, tightness, or obstructive signs seen with asthma. Consideration must also be given to gastroesophageal reflux disease, pneumonia, postnasal drip caused by allergic rhinitis, or bronchitis as alternate diagnoses. If the clinical picture is consistent with asthma, but reversibility of airway obstruction cannot be demonstrated, then a trial of asthma treatment can be used for diagnosis in pregnancy.¹

Interactions of Pregnancy and Asthma

Overall, the effect that pregnancy has on any one patient's asthma is unpredictable, and the likely intricate interaction of the immune changes of asthma on pregnancy is unclear. Possible mechanisms include maternal hormone changes and altered beta-adrenergic receptor responsiveness. Even fetal sex may play a role, with some data showing increased severity of symptoms in pregnancy with a female fetus.^{6,7} A large prospective study by Schatz and colleagues⁸ reported that asthma symptoms improved in pregnancy in 23% and worsened in 30%. This widely held rule of thirds (one-third of patients with asthma in pregnancy improving, one-third worsening, and one-third with no change) makes asthma in pregnancy the very definition of unpredictable.

In a large prospective study, rates of asthma exacerbation and hospitalization in pregnant patients with asthma were found to be directly proportional to the degree of severity classification. Patients with mild asthma were found to have an incidence of exacerbations at 12.6% with a hospitalization rate of 2.3%. Women with moderate asthma had an exacerbation rate of 25.7% and hospitalization rate of 6.8%. Women with severe asthma had an exacerbation rate of 51.9% and a hospitalization rate of 26.9%.⁸ Thus, knowing the classification of a patient's asthma is important in assessing her risk of exacerbation as well as the risk her asthma places on the outcome of pregnancy.

CLASSIFICATION OF ASTHMA SEVERITY AND CONTROL

Classification of a patient's asthma severity is important to help predict the possible risk of severe exacerbation and the need for maintenance therapy. Patients with mild asthma, who require regular medications, have the same number and severity of exacerbations as those with moderate asthma.⁸ Thus, the generalist obstetrician should be familiar with the classification, evaluation, and management of asthma in pregnancy.

Patients should be assessed at the first prenatal visit for history of exacerbations, hospitalizations, the use of oral steroids in the past, and the need for mechanical ventilation. For multiparous women, their asthma history in previous pregnancies should be reviewed. Schatz and colleagues noted that when subjects were assessed in successive pregnancies, 60% of them followed the same course with their asthma

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symptoms. Instruction in the use of a peak flow meter and recording of a baseline value should also be done at this early stage in pregnancy. If the patient is already aware of her personal best value, it should be recorded.

Table 1 presents the National Institutes of Health classification system for asthma severity.⁹ The preferred and alternative management strategies for each class of asthma in pregnancy are also included in this table. These classifications should be seen as a dynamic system in which, during a pregnancy, a patient may change classes and treatments several times. Knowing and applying the classification system is essential to selecting appropriate management as well as anticipating complications during pregnancy.

Patients with mild intermittent asthma, patients with mild persistent asthma, and selected patients with moderate persistent asthma can be treated adequately by the generalist obstetrician. Patients with severe asthma and those with moderate asthma that is increasingly complex require referral to a pulmonologist and a maternal-fetal medicine specialist for shared management of pregnancy and asthma.

ASTHMA MANAGEMENT

The ultimate goal of asthma therapy is to prevent hypoxic episodes to preserve continuous fetal oxygenation; improved maternal and perinatal outcomes are achieved with optimal control of asthma. One-third of women with asthma develop worsening of control during pregnancy, therefore close

monitoring and frequent reevaluation are essential. There are 4 important aspects of asthma treatment to ensure optimal control: (1) close monitoring, (2) education of patients, (3) avoidance of asthma triggers, and (4) pharmacologic therapy. Patients who are not responding adequately to treatment should have their level of treatment intensified.

Monitoring Asthma in Pregnancy

The reliability of subjective measures by patient or physician for asthma severity has not proven dependable. FEV1 has been shown to be a reliable objective measure of airway obstruction and correlates with pregnancy outcome.¹⁰ FEV1 measurement requires a spirometer, which is not available in most physicians' offices. The measurement of peak expiratory flow rate (PEFR) can easily be performed in the office at a prenatal visit using a peak flow meter, see figure 1. A PEFR meter is inexpensive and easy to use. PEFR should be performed with the patient standing and taking a maximum inspiration. The best value of 3 attempts is used for comparison with previous numbers.

Typical PEFR in pregnancy should be 380 to 550 L/min. Each individual patient should establish her personal best and that value should be recorded in the prenatal chart at the earliest prenatal visit. The caregiver can then provide the patient with a peak flow meter marked with 80%, 50% to 80%, and less than 50% of the patient's personal best. Patients should be advised that 80% or more of PEFR is considered

Asthma Severity	Mild intermittent asthma	Mild persistent asthma	Moderate persistent asthma	Severe Asthma
Overall control	Well controlled	Not well controlled	Not well controlled	Very poorly controlled
Symptoms Classification	<ul style="list-style-type: none"> ✓ Symptoms twice per week or less ✓ Nocturnal symptoms twice per month or less ✓ FEV₁ 80% of predicted or more 	<ul style="list-style-type: none"> ✓ Symptoms more than twice per week, but not daily ✓ Nocturnal symptoms more than twice per month ✓ FEV₁ 80% of predicted 	<ul style="list-style-type: none"> ✓ Daily symptoms ✓ Nocturnal symptoms more than once per week ✓ FEV₁ more than 60% to less than 50% predicted. ✓ Regular medications necessary to control symptoms 	<ul style="list-style-type: none"> ✓ Continuous symptoms ✓ Nocturnal symptoms are frequent ✓ FEV₁ 60% or less of predicted ✓ Regular oral corticosteroids necessary to control symptoms
Preferred management	<ul style="list-style-type: none"> ✓ No daily medications, albuterol as needed 	<ul style="list-style-type: none"> ✓ Low-dose inhaled corticosteroid such as budesonide or fluticasone ✓ Albuterol as needed 	<ul style="list-style-type: none"> ✓ Low-dose inhaled corticosteroid AND salmeterol -OR- ✓ Medium-dose inhaled corticosteroid and salmeterol if needed ✓ Albuterol as needed 	<ul style="list-style-type: none"> ✓ High-dose inhaled corticosteroid and salmeterol AND oral corticosteroid if needed ✓ Albuterol as needed
<p>For acute symptoms: Albuterol 2-6 puffs as needed for FEV1 less than 80%, exposure to allergens or exercise should supplement all treatment plans. May repeat in 20 minutes. If no response then patient should seek medical attention. May need a short burst of methylprednisone 40-60mg daily in a single or divided dose for 3-10 days, no taper needed</p>				
<p>Adapted from National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program. Expert panel report: guidelines for the diagnosis and management of asthma. NIH Publication No. 05-5236. Bethesda (MD): NHLBI. Available at http:// www.nhlbi.nih.gov/health/prof/lung/asthma/astpreg/astpreg_full.pdf</p>				

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Figure 1: Peak Flow Meter ¹¹

vice regarding changes in medication. At less than 50%, she should be seen immediately in the emergency department if necessary.

Patient Education

Patient education should begin at the first prenatal visit. Explanation of the importance of optimal asthma control and the risks of poor control for the patient and the fetus should be discussed early in pregnancy. Patients should be taught how to do peak flow measurements, how to record the results, and what values should be of concern, as well as who to contact in emergent situations. Patients should be observed using their inhalers and peak flow meters and correct use reinforced. Frank discussion about the importance of continuing asthma medications and the possible severe consequences for the patient and her fetus with discontinuation is vital.

Avoidance of Triggers

Up to 80% of patients with asthma have positive skin tests to allergens, the most common being animal dander, dust mites, cockroach antigens, pollens, and molds. There are non-immune triggers as well, including strong odors, tobacco smoke, air pollutants, and drugs such as aspirin and b-blockers. For exercise-triggered asthma, the use of a bronchodilator 5 to 60 minutes before exercise may reduce symptoms. Avoidance of these allergens and triggers can significantly reduce the need for medication and the occurrence of exacerbations during and after pregnancy. All patients should be strongly encouraged to stop smoking, but especially those with asthma because they are at increased risk for worsening chronic and acute asthma sequelae.

Pharmacotherapy

Medical therapy includes a stepwise approach in an attempt to use the least amount of medication necessary to control a patient's asthma and keep her severity in the mild range. Goals of therapy include having normal or near-normal pulmonary function and minimal or no chronic symptoms, exacerbations, or limitations on activities. The final goal is to minimize the adverse effects of treatment. It is safer for pregnant women with asthma to be treated with asthma medications than to have exacerbations or asthma symptoms.⁹ It is assumed that asthma medications are as effective in the pregnant patient as in the non-pregnant woman;

good control; however, optimal control in pregnancy is 90% to 100% of personal best.¹ The pregnant woman should be advised that if PEF is within the 50% to 80% range she should arrange an appointment to see her physician or obtain ad-

vice regarding changes in medication. At less than 50%, she should be seen immediately in the emergency department if necessary.

however, there may be physiologic changes in pregnancy that affect many aspects of the pharmacokinetics of these medications. The mainstay of therapy is to treat airway inflammation, to reduce hyperresponsiveness and prevent symptoms. Secondary therapy is aimed at treatment of exacerbations with bronchodilator therapy. At least twice during pregnancy, treatment should be reviewed and stepped up if symptoms are persistent; or, if symptoms are well controlled, therapy can be maintained or even decreased.⁹

Inhaled Corticosteroids

Inhaled corticosteroids (ICS) are preferred for the management of all levels of persistent asthma in pregnancy.⁹ Corticosteroids are the most effective treatment for the airway inflammation of asthma and reduce the hyperresponsiveness of airways to allergens and triggers. These medications have also been shown to decrease the incidence of exacerbations by more than threefold compared with those who do not use ICS.¹ Concern for risk of congenital malformations with ICS exposure in the first trimester has proved unfounded; multiple studies have confirmed their safety regardless of dose.¹²

The most well studied inhaled corticosteroid is budesonide.¹³ Because there are more data regarding this medication than other corticosteroids, budesonide is considered the preferred medication by the National Asthma Education and Prevention Program (NAEPP) and is US Food and Drug Administration (FDA) pregnancy category B. All other corticosteroids are category C. However, if a woman's asthma is well controlled on a different inhaled steroid, it is recommended that the regimen be continued.¹⁴

Inhaled β_2 Agonists

Inhaled β_2 agonists are recommended for asthma treatment for all classes of severity. Albuterol is the first-line rescue inhaler for the rapid relief of symptoms of acute bronchospasm. It should be noted that metered dose inhalers have recently been revised by manufacturers to eliminate chlorofluorocarbons, and to now use hydrofluoroalkane (HFA) as a propellant. Because of this change, many commonly used inhalers have new brand names, and generic forms may not be available (eg, Proventil to Proventil HFA, Schering-Plough Corporation). It is important to inquire at each prenatal visit how often the patient has needed to use her β_2 agonist inhaler.^{9,15} If a patient requires more than 2 inhalation treatments with a β agonist in a week, this indicates the need for an additional preventative maintenance agent such as ICS.

Leukotriene Moderators, Cromolyn and Theophylline

Leukotriene moderators, cromolyn and theophylline are alternative treatments for mild persistent asthma and adjunctive treatments for moderate and severe persistent asthma, but are not the preferred regimen.⁹

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Management of an Acute Asthma Exacerbation in Pregnancy

An asthma exacerbation in a pregnant woman places both mother and fetus at increased risk for a negative outcome because of the risk of severe hypoxemia during these events. The most important management of an acute exacerbation is prevention; however, Schatz and colleagues⁸ noted that 52% of patients with severe asthma have an exacerbation during pregnancy, and many of these women require hospitalization.

Initial evaluation in the emergency department or labor and delivery should be the same as for acute asthma in the nonpregnant state: measurement of PEF, and comparison with predicted or previously recorded best. Oxygen should be given and oxygen saturation kept higher than 95%. The goal of hospital management is reversal of bronchoconstriction with inhaled β_2 agonists and corticosteroids (oral or IV), prevention and correction of hypoxemia, or reduction of hypercarbia. Intensive care unit admission or intubation is indicated in those with life-threatening asthma, in those with PCO₂ higher than 40 to 45 mmHg on arterial blood gas, mental status changes, maternal exhaustion, respiratory acidosis, or fetal distress.

Possible differential diagnoses of a severe exacerbation unresponsive to initial treatment should include pulmonary edema, pulmonary embolism, cardiomyopathy, and amniotic fluid embolism.

Refractory status asthmaticus is defined as a severe exacerbation of asthma that is unresponsive to bronchodilators and corticosteroids and that requires intensive care unit admission and typically mechanical ventilation. In patients who require intensive care unit admission and intubation and who continue to have refractory life-threatening asthma despite aggressive treatment, delivery should be considered a therapeutic option; however, this is rarely required. A cesarean delivery is most likely necessary in these severe cases because of the urgency of the need for delivery. Information about the management of refractory status asthmaticus in obstetric patients is minimal and only available in the form of case series reports. Review of 3 case reports with a total of 10 cases, 2 of which were past 32 weeks, revealed 2 patients who underwent cesarean delivery and improved dramatically after the procedure.¹⁶⁻¹⁸

Improvement in a severe asthma exacerbation after delivery may result from several physiologic factors, including reduced pressure on the diaphragm and decreased oxygen consumption.¹⁹ Vaginal delivery may be possible during an acute exacerbation in the setting of progressive active labor, normal maternal oxygenation, absence of hypercapnea, adequate neuraxial anesthesia, and use of operative vaginal delivery. If delivery is being considered for maternal reasons at a gestational age between 24 and 34 weeks, then betamethasone should be given before delivery for fetal lung maturity if at all possible.

Management of Asthma During Labor and Delivery

Asthma medications should not be discontinued or delayed during labor and delivery. Although asthma during labor is typically quiescent, consideration should be given to obtaining a peak flow measurement on admission and then every 12 hours or as needed to monitor for asthma exacerbation. Monitoring is likely only necessary in those women who have a history of exacerbations during pregnancy. Neuraxial anesthesia decreases oxygen requirements and minute ventilation and thus can be helpful for control of asthma symptoms during labor. If systemic (oral or intravenous) corticosteroids have been used in the previous 4 weeks for treatment longer than 10-14 days, then the patient should receive stress-dose steroids to prevent an adrenal crisis. Usually, this regimen begins with hydrocortisone 100 mg every 8 hours, continued for 24 hours post partum, and then stopped. Tapering stress steroids is not necessary.

Medications typically used for tocolysis, induction of labor, and during delivery can have an influence on asthma symptoms, especially in the most severe or medication sensitive asthmatic patients. Prostaglandins E₂ or E₁ can be used for cervical ripening, for post partum hemorrhage or to induce abortion without significant adverse reaction.²⁰ In these cases, respiratory status of the patient should be monitored in a routine fashion. Carboprost (prostaglandin F_{2 α}), ergonovine, and rarely methylegonovine can cause bronchospasm, especially in the aspirin-sensitive patient.²¹⁻²² For these patients, choosing a medication such as misoprostol, which is an E₁, may be more appropriate.

Magnesium sulfate is a bronchodilator, and should not have a deleterious effect on asthma, but indomethacin can induce bronchospasm in an asthmatic patient with known aspirin sensitivity. No formal studies on calcium channel blockers in the asthmatic gravid patient have been published, but bronchospasm has not been observed with the wide clinical use of these medications for tocolysis.

Breastfeeding

Asthma medications are excreted in small and varying amounts into breast milk. The NAEPP found that there was no contraindication for the use of prednisone, theophylline, cromolyn, antihistamines, ICS, or inhaled β agonist for breastfeeding.⁹ Patients should be instructed, and strongly encouraged, to continue their asthma medications post partum with or without breastfeeding.

SUMMARY

Asthma is a chronic illness that complicates a significant number of pregnancies. Generalist obstetricians should be familiar with its diagnosis, classification, treatment, and possible complications in pregnancy. Providers should instruct and strongly urge patients to remain on asthma medications during pregnancy because one-third of patients have worsening of their asthma, including those women with mild asthma. There are proven negative effects from exacerbations

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and poor control on pregnancy outcome, whereas there are clear benefits of good control. Patient education about the importance of good asthma control is essential for improving compliance and self-monitoring.

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