Chapter 1

Asthma in Pregnancy

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Asthma is a chronic inflammatory disease of the airways that is characterized by increased responsiveness of the tracheobronchial tree to multiple stimuli. Asthmatics are more responsive than nonasthmatics to a wide range of triggers, leading to increased inflammatory markers which leads to excessive narrowing with consequent reduced airflow and symptomatic wheezing and dyspnea. Narrowing of the airways is usually reversible, but in some patients with chronic asthma may be irreversible airflow obstruction. It is the most common chronic condition in pregnancy.

The disease is episodic, being characterized by acute exacerbations with symptom-free periods. Most asthma attacks prove to be short-lived, lasting minutes to hours. Bronchodilator influences are due to progesterone and cortisol and bronchoconstriction influences are due to reduced residual volume and increased PGF_2 and thromboxane. Asthma increases maternal morbidity. There have been multiple genes, chromosomal regions, and epigenetic changes associated with the development of asthma. Racial and ethnic differences have also been reported in asthma and are likely the result of a complex interaction between genetic, socioeconomic, and environmental factors.

PATHOPHYSIOLOGY

Asthma is characterized by airway obstruction, hyperinflation, and airflow limitation resulting from multiple processes.

Physiological factors affecting asthma in pregnancy:

1. Increase in free cortisol levels may protect against inflammatory triggers.
2. Increase in bronchodilating substances (such as progesterone) may improve airway responsiveness.
3. Increase in bronchoconstricting substances (such as prostaglandin F2a) may promote airway constriction.
4. Placental 11β-hydroxysteroid dehydrogenase type 2 decreased activity is associated with an increase in placental cortisol concentration and low birth weight.
5. Placental gene expression of inflammatory cytokines may promote low birth weight.
6. Modification of cell-mediated immunity may influence maternal response to infection and inflammation.

Clinical Course

Recurring episodes of cough, dyspnea, chest tightness, and wheezing are suggestive of asthma. Symptoms are often worse at night or early morning, in the presence of potential triggers, and/or in a seasonal pattern. A personal or family history of atopy can increase the likelihood of asthma. Maternal risk increases with status asthmaticus. Life-threatening complications include pneumothorax, cor pulmonale, cardiac arrhythmias and respiratory failure.

Effects of Pregnancy on Asthma

Pregnant asthmatic women 1/3 feel better (23%), 1/3 no change, 1/3 worse (30%). Women with severe asthma tend to have worsening of their asthma.

1. Asthma exacerbations can occur at any time during gestation but increase between 17 and 36 weeks gestation (mean 25 weeks) less severe during last 4 weeks.
2. In women whose asthma worsened, the increase in symptoms was most prominent between week 29 and 36 of gestation. Asthma was generally less severe during the last 4 weeks of pregnancy.
3. In women who improved, the improvement was gradual as pregnancy progressed.
4. Substantial asthma symptoms were uncommon during labor and delivery.
5. The course of asthma in successive pregnancies in an individual patient tended to be similar. Respiratory viral infections were the most frequent triggers of exacerbations (34%), followed by poor adherence to inhaled corticosteroid therapy (29%). Therefore, during pregnancy women with asthma need to be closely reviewed throughout pregnancy, irrespective of disease severity.

Effects of Asthma on Pregnancy

If asthma is not controlled, women may be at increased risk for pre-eclampsia. This points to a mechanistic common pathway of mast cell–airway smooth muscle cell interactions. There is twofold increase in preterm delivery among pregnancies complicated by asthma compared to nonasthmatic controls. Retrospective and prospective studies have demonstrated that women with asthma have a higher frequency of cesarean section than women without asthma.

Neonatal Outcome

Neonatal hypoxia, low birth weight, preterm birth associated with impaired function of developing organs such as the central nervous system or kidney, small for gestational age (IUGR), congenital anomalies especially first trimester exposure (e.g. cleft palate especially with triamcinolone), perinatal morbidity and mortality. Poorly controlled asthma has been associated with 15 to 20% increase in both maternal and fetal risks. These risks are increased 30 to 100% those with more severe asthma. Asthma is not associated with risk of congenital malformations, it is associated with medication used during pregnancy.

Preconceptional Care

Overall risk of any child having asthma is about 4%, if one parent have asthma the risk increases 8–16% and with both parents its risk increases high as 30%. Optimize asthma management. Avoid recently introduced medications whose safety in pregnancy is not established. Use adequate doses of medications to control symptoms and avoid hypoxia. It is essential to maintain adequate oxygenation to the fetus.

Clinical Evaluation

Asthma is diagnosed by spirometry. This can help to differentiate shortness of breath is a common complication of pregnancy or if it is caused by asthma. If asthma is under control and mild, no special tests needed. In moderate to severe asthma periodic ultrasounds are done to check baby's growth. Test results can alert growth defects.

Laboratory Evaluation

Lung function tests: Simple spirometry confirms airflow limitation with a reduced FEV1, FEV1/FVC ratio, and PEF. Reversibility is demonstrated by >12% and 200 ml increase in FEV1 15 min after an inhaled short-acting β_2-agonist.

Airway responsiveness: The increased AHR is normally measured by methacholine or histamine challenge with calculation of the provocative concentration that reduces FEV1 by 20%.

Hematologic tests: Blood tests are not usually helpful. Total serum IgE and specific IgE to inhaled allergens (radioallergosorbent test [RAST]) may be measured in some allergic asthma prone patients.

Imaging: Obtaining a CXR is not routinely required and is performed only where pneumonia or pneumothorax, is suspected or to rule out other causes of respiratory symptoms in patients being evaluated for asthma. CT of the chest can be considered in patients with severe asthma refractory to treatment to evaluate for alternative diagnosis.

Skin tests: Skin prick tests to common inhalant allergens such as house dust mite, cat fur, grass pollen.

An objective measurement of airflow obstruction is essential to the evaluation of an exacerbation. The severity of the exacerbation should be classified as:

- Mild (PEF or FEV1 >70% of predicted or personal best)
- Moderate (PEF or FEV1 40–69%)
- Severe (PEF or FEV1 <40%)
- Life-threatening/impending respiratory arrest (PEF or FEV1 <25%)

Management of Chronic Asthma

It is important to maintain good control of asthma because poor control may have adverse effects on fetal development. Compliance is a major problem because there is often concern about the effects of antiasthmatic medications on fetal development. The drugs that used for many years in asthma therapy have now been shown to be safe and without teratogenic potential. These drugs include SABA, ICS, and theophylline; regarding the newer class of drug there is less safety information about drugs such as LABA, antileukotrienes, and anti-IgE. If an oral corticosteroid is needed, it is better to use prednisone rather than prednisolone because it cannot be converted to the active prednisolone by the fetal liver, thus protecting the fetus from systemic effects of the corticosteroid. There is no contraindication to breastfeeding when patients are using these drugs by inhalational route.

Oral corticosteroids have possible increased risks like oral clefts, prematurity, lower birth weight in pregnancy. These risks are less than the potential risks of severe uncontrolled asthma (which include maternal or fetal mortality) so should be used in cases where need arises.

Tiotropium has been found effective in nonpregnant patients uncontrolled by inhaled corticosteroids and long-acting β-agonists (ICS/LABA) combination drugs. Although no human pregnancy safety data have been published for tiotropium, animal studies have been reassuring.

Management of Acute Asthma

Most important aspect is to avoid asthma triggers to minimize hyperresponsiveness and airways inflammation after that oxygen inhalation to maintain oxygen saturation >95%. Nebulization with high dose Albuterol every 20 minutes along with inhaled ipratropium bromide and systemic corticosteroid with repeated assessment. IV corticosteroids 200 mg stat repeated after 4 hours to be used along with β_2-agonists due to longer onset of action of steroids. Patients with FEV1 or PEFR <50% and pCO_2 >42 mm Hg needed intubation and mechanical ventilation with 100% oxygen in ICU.

Systemic corticosteroids (40–80 mg/day in one or two divided doses) are recommended for patients who do not respond well (FEV, or peak expiratory flow rate [PEF] less than 70% predicted) to the first β-agonist treatment as well as for patients who have recently taken systemic steroids and for those who present with severe exacerbations (FEV, or PEF less than 40% of predicted). Patients with good responses to emergency therapy (FEV, or PEF 70% or greater of predicted) can be discharged home, generally on a course of oral corticosteroids. Inhaled corticosteroids should also be continued or initiated upon discharge until review at medical follow-up. Hospitalization should be considered for patients with an incomplete response (FEV, or PEF 40% or greater but 70% or less than predicted). Admission to an intensive care unit should be considered for patients with persistent FEV, or PEF 40% or less of predicted, pCO_2, 42 or greater or sensorium changes. Intubation and mechanical ventilation may be required for patients whose condition deteriorates or fails to improve associated with decreasing pO_2, increasing pCO_2, progressive respiratory acidosis, declining mental status or increasing fatigue.

- β_2-Agonist bronchodilator (nebulized or metered-dose inhaler) up to 3 doses in first 60–90 minutes
- Every 1–2 hours thereafter until adequate response
- Nebulized ipratropium (may be repeated every 6 hours)

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Systemic corticosteroids with initial therapy in patients on regular corticosteroids and in patients with severe exacerbations (peak expiratory flow rate less than 40% predicted or personal best) and for those with incomplete response to initial therapy 40–80 mg/day in 1 or 2 divided doses until peak expiratory flow rate reaches 70% of predicted

- orally or IV for severe exacerbation
- taper when patient condition improves

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Intravenous magnesium sulfate (2 g) can be given for women with life-threatening exacerbations (peak expiratory flow rate less than 25% predicted or personal best) and whose exacerbations remain in the severe category after 1 hour of intensive therapy.

Obstetrical Management

During pregnancy, patients should have more frequent follow-up because the severity of asthma often changes and requires supportive medication adjustment. There is more potential risk to the fetus with poorly controlled asthma than with exposure to asthma medications, most of which are generally considered safe. A recent birth cohort study of ICSs in pregnant women with asthma confirmed their safety. Clinical evaluation of patient in labor may be inaccurate to

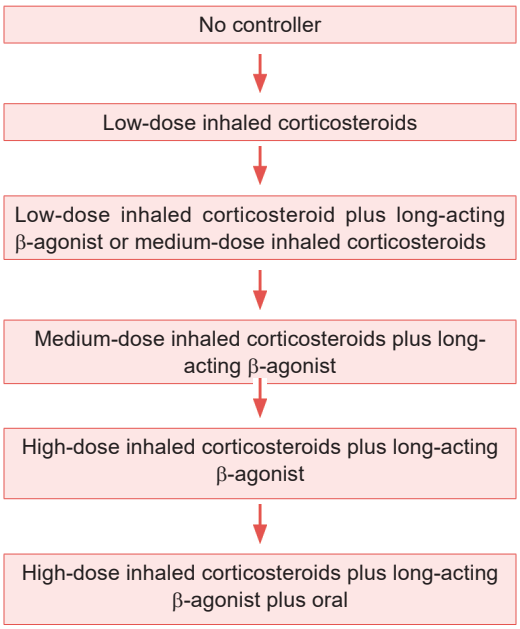
predict the severity of asthma thus PEFR or FEV1 should be determined. Asthma medication to be continued FEV1 >70% and fetal status.

Obstetrical management of pregnant with asthma: In case of cesarean section. Lumbar epidural analgesia should be used as it decreases O_2 consumption and minute ventilation. Fentanyl to be used as a narcotic analgesic and if general anesthesia required ketamine is preferred. In case of labor oxytocin and prostaglandin E_2 suppositories for labor induction and pitocin, misoprostol for postpartum hemorrhage is used. Drugs to be avoided during obstetrical management are morphine, meperidine,15-methylprostaglandin F2α and ergot alkaloids. Whole delivery team should be made aware of existing asthma, particularly anesthetist.

Postpartum period: In the postpartum period there is no increased risk of asthma exacerbations and within a few months after delivery a woman's asthma severity typically reverts to its pre-pregnancy level.

Nonsteroidal anti-inflammatory drugs (NSAIDs) for analgesia are to some degree contraindicated in asthma and may cause bronchospasm but in women without intolerance to NSAIDs they can be used.

Women with severe disease, particularly if systemic corticosteroids are considered, need respiratory physicians. Exclusive breastfeed for at least 6 months is recommended.



KEY POINTS

- Labor induced with PGE_2 (Cerviprime gel) or PGE_1 analogue (misoprostol)
- Tiotropium can be used in pregnant women whose asthma is not controlled by ICS/LABA.
- Few data are available on the safety of asthma drugs in breastfed neonates, but in general the same medications safe in pregnancy can be continued. Those with uncertain safety profile should be avoided.
- Breastfed children have a reduced risk of developing allergic disease including asthma is unproven, but this does not outweigh the benefit of breastfeeding.