Managing Asthma during Pregnancy

Jennifer Namazy MD

Clinical Professor of Medicine

Division of Allergy and Immunology

Scripps Clinic

La Jolla, California

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Learning Objectives

1. Understand how optimal management can improve maternal and fetal outcomes
2. Identify steps associated with effective management of asthma during pregnancy using objective measures of asthma control, patient education and importance of care coordination
3. Review the safety of commonly used medications during pregnancy

Case

28 year old woman (gravida 1 parity 0)

Estimated 11 weeks gestation

History of asthma diagnosed at age 2

Complains of dyspnea, wheezing and nighttime awakenings caused by cough

Recently prescribed an inhaled corticosteroid

Concerned about restarting asthma medications because of possible effects on her unborn baby

Prevalence

- In the US **5.3%** of pregnant individuals have asthma (2018) and the prevalence is increasing
- **40%** of women have worsening symptoms during pregnancy while 60% have no change in symptoms.
- Two large US healthcare claims databases found 19% had severe asthma(privately insured)
- At least **20%** of women experience an exacerbation during pregnancy
- May increase the risk of perinatal complications
- **Optimal management improves maternal and fetal outcomes**

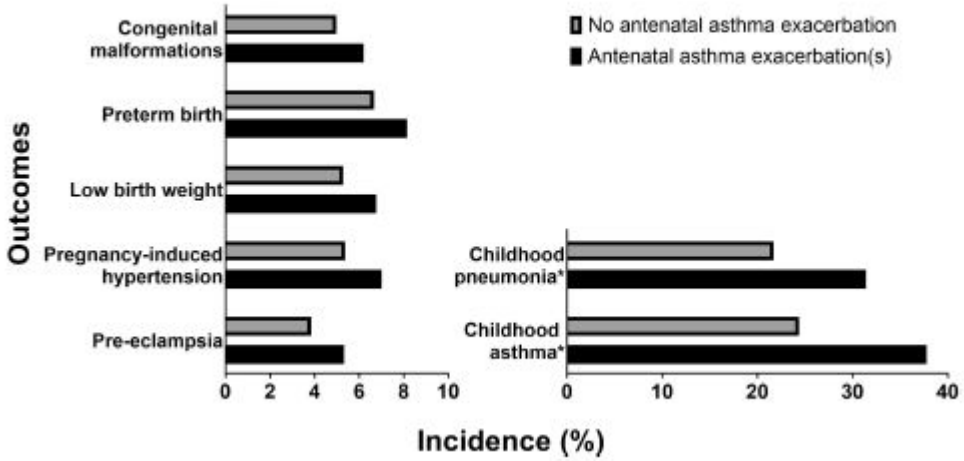
Murphy et al. JACI-IP.2023

Effect of Asthma on Pregnancy

Outcome	No. of Studies	Result
Preeclampsia	15	1.54 (1.32-1.81)
Preterm birth	18	1.41 (1.23-1.62)
Low birth weight	13	1.46 (1.22-1.75)
SGA	11	1.22 (1.14-1.31)
Neonatal death	6	1.49 (1.11-2.00)
Malformations	12	1.11 (1.02-1.21)

Murphy, et al. *BJOG* 2011; 118:1314 and *BJOG* 2013; 120:812

Effect of Asthma on Pregnancy



Couillard et al. Obstet Med 2021

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Case

The relationship between asthma and pregnancy and the risk of untreated asthma was discussed with the patient

She was told that pregnant asthmatics have a higher risk of complications

Those women with uncontrolled asthma have an even greater risk

Variable	Well-controlled	Not well-controlled	Very poorly controlled
Sx frequency	≤ 2 days/week	> 2 days/week	Throughout the day
Nocturnal Sx	≤ 2 times/month	1-3 times/week	≥ 4 times/ week
β agonist use	≤ 2 days/week	> 2 days/week	Several times/day
Activity interference	None	Some	Extreme
FEV_1/PEF	> 80 %	60-80 %	< 60 %

Schatz and Dombrowski. *NEJM* 2009; 360:1862

Case

In the last two years she has received 2 courses of oral corticosteroids for acute attacks of asthma

One of these episodes occurred after she had visited a friend's house with 2 cats

She says her asthma symptoms have been more frequent since that episode

She requires albuterol 2 -3 times a day and her symptoms are interfering with sleep

Managing asthma during pregnancy

- Assessment and Monitoring
- Reduction of triggers
- Patient education
- Pharmacologic therapy

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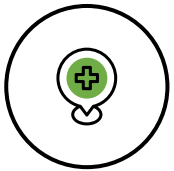
Adherence



Mother To Baby adherence survey to 396 participants

- **Most agreed it was important to control asthma(90%)**
- **Lack of adequate information on safety of medications(45%)**
- **Concern of side effects(15%)**
- **12% believe that asthma medications are unsafe**

Discuss in a non-judgmental way

- Identify barriers and possible solutions
- Observe and correct inhaler technique
- Provide effective reassurance regarding the risks of asthma medications during pregnancy, especially compared to the risks of uncontrolled asthma
- Collaborate on the treatment plan
- Implement effective follow-up

We can do better….

A recent survey showed that :

- 36% of pregnant women did **NOT** have their asthma reviewed during their pregnancy
- Only 31% had a written asthma plan
- 11% had lung function assessed
- 65% not questioned about asthma symptoms

McLaughlin et al. Women Birth.2022

Health Disparities During Pregnancy

- African American and Hispanic women are more likely to have asthma in cohorts of pregnant women
- African American women are more likely to have asthma exacerbations during pregnancy
- Infants of African American women are more likely to be preterm and low birthweight
- Insurance and access to healthcare can contribute to worse asthma control
- **Need to provide culturally tailored asthma programs to patients.**

Asthma management improves outcomes

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- Improves asthma control
- Reduces exacerbations
- Improves quality of life

Self Management

- Assessment of **asthma control** using objective measures
  - Structured asthma history using a validated questionnaire (**p-ACT**)
- **Patient Education**
  - Written asthma action plan
  - Address concerns and risks of medication discontinuation

Murphy et al.CHEST.2022

Asthma self management education

ELSEVIER

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

An observational study of the impact of an antenatal asthma management service on asthma control during pregnancy

L.E. Grzeskowiak[a], B. Smith[b], A. Roy[b], G.A. Dekker[a], V.L. Clifton[a,c,*]

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- Prospective observational cohort study
- Nurse-led antenatal asthma management and education
- Reduced asthma exacerbations and uncontrolled asthma

Multidisciplinary approach to care

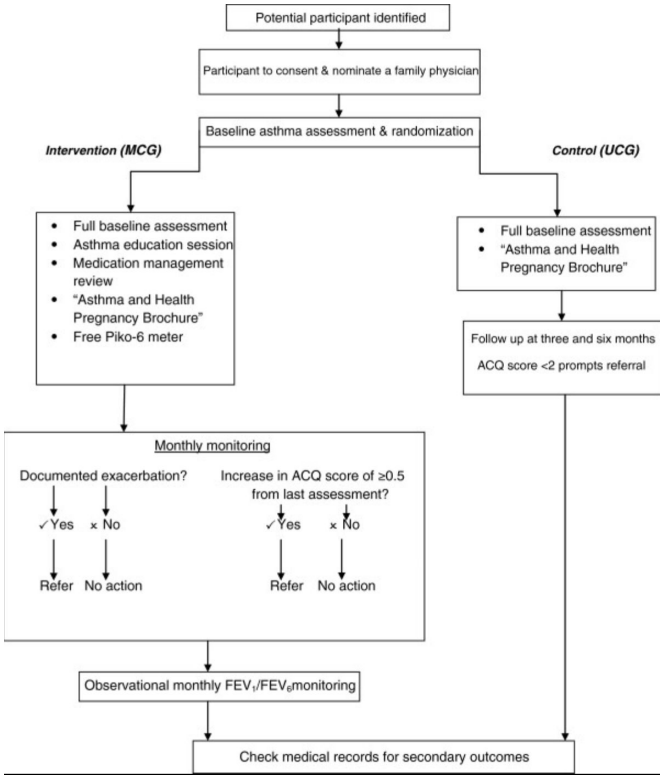
CHEST®

Volume 145, Issue 5, May 2014, Pages 1046-1054

Original Research

Multidisciplinary Approach to Management of Maternal Asthma (MAMMA): A Randomized Controlled Trial

Angelina S. Lim BPharm (Hons) [a], Kay Stewart PhD [a], Michael J. Abramson PhD [b], Susan P. Walker MD [c, d], Catherine L. Smith MSc [b], Johnson George PhD [a]



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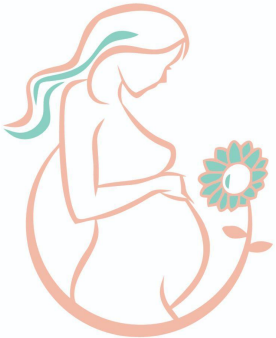
Shared Decision Making

“Develop a partnership”

- Give opportunities to express concerns
- Encourage patients to participate in their care
- Provide information for patients to understand their asthma
- Decisions about treatment can be negotiated
- Goal setting

Integrated care works!

- Care coordination among pregnant individuals and all of those who care for them



Breathe 4 Baby ToolKit

- A program that will include an action plan for pregnant asthmatic patients that can be used to coordinate care between healthcare providers including allergists, pulmonologists, and obstetricians caring for pregnant asthmatics.
- This resource will create a foundation of support that would enhance multidirectional communication and promote better care for pregnant asthmatic women.

Collaboration

- COORDINATION
- FOUNDATION
- DISSEMINATION

aafa Asthma and Allergy Foundation of America

VAMPSS Vaccines and Medications in Pregnancy Surveillance System

AAAAI American Academy of Allergy Asthma & Immunology

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American Academy of Allergy Asthma & Immunology

Asthma and Allergy Foundation of America

PREGNANCY AND LACTATION ASTHMA ACTION PLAN

Name: _____ Date: _____

Emergency Contact: _____ Relationship: _____

Cell phone: _____ Work phone: _____

Health Care Provider: _____ Phone number: _____

Frequency of asthma check-up visits: _____ Personal Best Peak Flow: _____

Name of asthma biologic (if any): _____ Dates of ultrasound for growth: _____

Biophysical profile recommended: Y____ N____ Date of last COVID-19/flu vaccine: _____

GREEN ZONE:

Doing Well with all of these

- ✓ No coughing, wheezing, chest tightness, or difficulty breathing
- ✓ Can work, play, exercise, perform usual activities without symptoms
- ✓ Good fetal movements

Take these medicines for control and maintenance:

Medicine	How much to take	When and how often

YELLOW ZONE:

Caution/Getting Worse if you have any of these

- ✓ Coughing, wheezing, chest tightness / pain, or difficulty breathing
- ✓ Symptoms with daily activities, work, play, and exercise
- ✓ Nighttime awakenings with symptoms
- ✓ Reduced fetal movements

CONTINUE your Green Zone medicines PLUS take these quick relief/rescue medicines:

Medicine	How much to take	When and how often

Call your doctor if you have been in the Yellow Zone for more than 24 hours.
Also call your OB immediately if there are reduced fetal movements.

RED ZONE:

Alert if you have any of these!

- ✓ Difficulty breathing, coughing, wheezing not helped with medications
- ✓ Trouble walking or talking due to asthma symptoms
- ✓ Not responding to quick relief medication
- ✓ Headache, vomiting
- ✓ Vaginal bleeding

FOR EXTREME TROUBLE BREATHING/SHORTNESS OF BREATH GET IMMEDIATE HELP!

Take these quick relief/rescue medicines:

Medicine	How much to take	When and how often

GO to the hospital/emergency department or CALL for an ambulance NOW!

American Academy of Allergy Asthma & Immunology
www.aaaai.org

PREGNANCY ASTHMA CONTROL TEST

1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work or at home?

All of the time	Most of the time	Some of the time	A little of the time	None of the tim
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. During the past 4 weeks, how often did you have shortness of breath due to your asthma?

More than once a day	Once a day	3 to 6 times a week	Once or twice a week	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?

4 or more nights a week	2 or 3 nights a week	Once a week	Once or twice	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?

3 or more times per day	1 to 2 times per day	2 to 3 times per week	Once or twice	Not at all
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. How would you rate your asthma control during the past 4 weeks?

Not controlled at all	Poorly controlled	Somewhat controlled	Well-controlled	Completely controlled
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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Pregnant with asthma? Know your asthma zones.

GO ZONE Doing Well:

No symptoms

Good fetal movements

CAUTION ZONE Getting worse if you have any of these:

Coughing, wheezing, or difficulty breathing

Waking up at night with symptoms

Chest tightness or pain

Reduced fetal movements

DANGER ZONE Alert your doctor if you have any of these:

Difficulty breathing, coughing, wheezing, and chest tightness or pain are getting worse

Headache

Vomiting

Trouble walking or talking

Vaginal bleeding

Medicine is not working

Knowing your asthma zones can improve the health of you and your baby!

aafa Asthma and Allergy Foundation of America

AAAAI American Academy of Allergy Asthma & Immunology

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What other information is included in the toolbox?

- Asthma and Pregnancy Basics
- Asthma medication fact sheets
- Patient-facing information about allergy immunotherapy
- A downloadable chart on the safety of asthma BIOLOGICS used during pregnancy

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aaaai.org/practice-management/practice-tools/asthma-and-pregnancy-toolkit
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Asthma and Pregnancy Toolkit
Breathe 4 Baby
Asthma and allergic diseases are the most common medical conditions faced during pregnancy. Asthma prevalence in pregnancy is 8-9% and increasing. Pregnant people with asthma have an increased risk for perinatal complications including preterm birth, low birth weight, and pre-eclampsia. Severe asthma in pregnancy is a cause of mortality. Optimal asthma management in pregnancy is associated with improved outcomes in maternal and fetal health.
The Breathe 4 Baby Toolkit is a resource for educating patients and providers regarding asthma prevalence, diagnosis, and management in pregnancy to improve outcomes for pregnant people with asthma and their babies. This includes the Pregnancy and Lactation Asthma Plan, the validated pregnancy ACT (p-ACT), and other educational resources.
Pregnancy and Lactation Asthma Plan
PLAN DE ACCIÓN CONTRA EL ASMA DURANTE EL EMBARAZO Y LA LACTANCIA (Pregnancy and Lactation Asthma Plan)
Pregnancy Asthma Control Test
PRUEBA DE CONTROL DEL ASMA DURANTE EL EMBARAZO (Pregnancy Asthma Control Test)
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The Compounding Corner

Breathe for Baby:
A Multidisciplinary Educational Program on Managing Asthma During Pregnancy and Lactation

- Develop healthcare curricula to address gaps in asthma management and care for people with asthma during pregnancy and lactation.
- Incorporate sustainable healthcare education practices into medical education while promoting the need for further research opportunities on asthma during pregnancy and lactation.
- Examine the effect of health disparities on sex/gender and race/ethnicity during pregnancy and lactation

Case

She agreed to start inhaled budesonide (180 mcg 2 puffs twice a day)

She was instructed on technique but has several questions regarding the safety of this medication during pregnancy

Low dose ICS + LABA

Table 2. Steps of Asthma Therapy during Pregnancy.*

Step	Preferred Controller Medication	Alternative Controller Medication
1	None	—
2	Low-dose inhaled corticosteroid	LTRA, theophylline, or cromolyn
3	Medium-dose inhaled corticosteroid	Low-dose inhaled corticosteroid plus LABA, LTRA, or theophylline
4	Medium-dose inhaled corticosteroid plus LABA	Medium-dose inhaled corticosteroid plus either LTRA or theophylline
5	High-dose inhaled corticosteroid plus LABA	—
6	High-dose inhaled corticosteroid plus LABA plus oral prednisone	—

Medium dose ICS+LABA+tiotropium

Biologic Therapy

* Data are from the National Asthma Education and Prevention Program.[24,25] We have modified step 3 to reflect the choice of a medium-dose inhaled corticosteroid over a low-dose inhaled corticosteroid plus a long-acting β-agonist (LABA) because of the lack of safety data on the use of LABA during pregnancy. LTRA denotes leukotriene-receptor antagonist.

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Schatz et al. NEJM. 2009

The NEW ENGLAND JOURNAL of MEDICINE

The Problem…and the consequence

- For the majority of new medications marketed in the U.S., there are inadequate or no human safety data available for pregnancy or lactation - ***refer to pregnancy registries!***
- Clinicians and patients have to make critical clinical decisions about treatment without adequate safety information available
- This leads to **undertreatment and poor adherence**, potentially leading to worse outcomes

Safety of specific asthma medications during pregnancy

- **SABA** are generally safe, albuterol has the most data, small studies show increased risk of certain specific congenital malformations, but asthma control and exacerbations are a confounder.
- **ICS** generally safe, especially low and medium dose. High dose reported to be associated with congenital malformations, but this observation may be confounded by control/severity. Most data for budesonide and fluticasone.
- **LABA** also likely safe. Data available for salmeterol and formoterol but less so than SABA and ICS Some reports of increased risk of specific malformations but asthma control/severity is a confounder.
- **LTRA** – most data for montelukast. No increased risk of congenital malformations. Possible increased risk of preterm birth, preeclampsia, gestational diabetes and low birth weight.
- **OCS** – use if indicated as maternal and fetal risk from uncontrolled asthma exceeds risk of OCS. Have been associated with congenital malformations, preeclampsia, gestational diabetes, low birth weight, neonatal adrenal insufficiency. Presence of cofounders – other asthma medication asthma severity.

Biologics

All of the asthma biologics are derivatives of IgG and differ in structure, placental passage and half life

- Monoclonal antibodies are transported across the placenta during the third trimester

Most mAb have the Fc domain of human IgG1 – Dupilumab and Reslizumab have IgG4 antibody framework

Suzuki,et al.J Immunol. 2010;184:1968-1976

Safety of Omalizumab

EXPECT is a single arm observational study to evaluate pregnancy outcomes in women exposed to omalizumab

Interim Data:

188 pregnant women

Rate of preterm birth, small for gestational age,low birth weight, major congnital malformations similar to those reported for pregnant severe asthmatics.

Final Data:

228 pregnant women compared to a disease-matched comparator population of pregnant women with moderate to severe asthma

No increased risk of major congenital malformations

Consider continuing in patients with a good response before pregnancy

Namazy et al. JACI 2015

Namazy et al. JACI 2019,

Other Biologics used in Asthma

- Nucala
- Fasenra
- Dupixent
- Tezspire

Recommendations on the use of Biologics during pregnancy

- Studying the safety of biologics is a challenge because of the relative infrequency of their use.
- Continue biologics in patients who are responding to them prior to pregnancy.
- Consider starting biologics during pregnancy in women who 1) are candidates for the therapy, and 2) who have severe asthma and are at risk of asthma exacerbations or oral corticosteroid use.
- One method to address research gaps regarding the safety of asthma biologics would be to increase awareness of pregnancy registries

Case

She was seen in clinic every 1-2 weeks initially to ensure that asthma control was improving

Once control had been achieved was followed on a monthly basis for review of symptoms and adherence to treatment as well as pulmonary function testing

Monitoring Asthma During Pregnancy

- Primary assessment - identify risk factors and start education
- Monitoring frequency
  - Higher risk patients evaluated at least once in 2nd trimester
  - Uncontrolled asthmatics followed every 6 weeks
- Systematic monitoring
  - p-ACT,ACQ, asthma plans, telemedicine

Bendien et al.JACI-IP.2024

Conclusion

- Uncontrolled maternal asthma may increase the risk of adverse perinatal outcomes
- For most medication used for any condition in pregnancy there are often limited or no data available
- Chance and confounding by disease severity /control may explain many of the positive associations
- Recommended asthma medications have reassuring safety data during pregnancy