Asthma in pregnancy

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ABSTRACT

Background: *Asthma is a frequent and potentially life-threatening disease that complicates many pregnancies. There are extensive data with regard to the diagnosis and treatment of asthma during pregnancy. Medical providers require an up-to-date summary of the critical aspects of asthma management during pregnancy.*

Objective: *This review aimed to summarize the available data from clinical trials, cohort studies, expert opinions, and guideline recommendations with regard to asthma in pregnancy.*

Methods: *A search through PubMed was conducted by using keywords previously mentioned and MeSH (Medical Subject Headings) terminology. Clinical trials, observational studies, expert opinions, guidelines, and other reviews were included. The quality of the studies was assessed, and data were extracted and summarized.*

Results: *Asthma worsens in ~40% of pregnant women, which can be associated with maternal and fetal complications. Physiologic changes in the respiratory, cardiovascular, and immune systems during pregnancy play a critical role in the manifestations of asthma. The diagnosis and the treatment of asthma are similar to that of patients who are not pregnant. Nonetheless, concern for fetal malformations, preterm birth, and low birth weight must be considered when managing pregnant patients with asthma. Importantly, cornerstones of the pharmacotherapy of asthma seem to be safe during pregnancy.*

Conclusion: *Asthma in pregnancy is associated with adverse outcomes. Roadblocks to management include associated comorbidities, medication nonadherence, atopy, lack of education, and smoking habits. These need to be acknowledged and addressed for successful asthma management during pregnancy.*

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Asthma prevalence during pregnancy ranges from 3% to 6%.[1] Among those pregnancies, 19% had severe asthma and 16% had poorly controlled asthma.[1] Furthermore, asthma is one of the most common chronic diseases that complicate pregnancies. However, approximately a fourth of pregnant patients with asthma discontinue their medications due to negative beliefs about safety.[2,3] Due to the extensive list of complications in pregnant patients with asthma and their fetuses, medical providers require an updated summary of key aspects in physiologic changes, diagnosis, and treatment. This review aimed to summarize the most recent data to assist the reader in the diagnosis and treatment of pregnant women with asthma. For this, we have gathered information from clinical trials, observational studies, expert opinions, guidelines, and other reviews. Institutional review board approval was not required.

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RELEVANT PHYSIOLOGIC CHANGES DURING PREGNANCY

A myriad of cardiovascular changes occurs in response to increased metabolic demands from the mother and fetus to ensure proper uteroplacental circulation. In the first trimester, there is a diminished peripheral vascular resistance,[4] with an increased cardiac output[5] and heart rate.[4] Also, oxygen and metabolic rate consumption increase by 20%.[6] Moreover, the respiratory system also undergoes adaptations during pregnancy with significant anatomic and hormonal changes that affect pulmonary function parameters in the mother.[7] As pregnancy progresses, there is an upward displacement of the diaphragm with an increased lower chest wall circumference and costal angle widening.[8] As a consequence, expiratory reserve and residual volumes decrease, while tidal volume increases.[9]

In contrast, forced vital capacity and peak expiratory flow do not change.[10] Interestingly, these changes are not associated with a significant deterioration of quality of life.[11] In addition, the elevation of progesterone levels, especially at the end of the first trimester, induces hyperventilation and results in a decreased (partial pressure of carbon dioxide; $PaCO_2$) with transient respiratory alkalosis.[12] Due to these physiologic changes, 60%–70% of pregnant women can experience dyspnea

Table 1 **Summary of physiologic changes during pregnancy**

System	Comment
Cardiovascular	Cardiac output increases while systemic vascular resistance and blood pressure decrease; red blood cells and plasma volume increase
Respiratory	Progesterone induces hyperventilation with subsequent changes in $PaCO_2$ and contributes to the physiologic dyspnea of pregnancy; as the gravid uterus enlarges and diaphragm displacement occurs, functional residual capacity decreases by 20%*: FVC, FEV_1, and PEF do not change, which makes spirometry variables used for asthma diagnosis comparable between pregnant and nonpregnant patients
Immune	Implantation is characterized by a predominant proinflammatory chemokine release with a subsequent anti-inflammatory environment to ensure fetal development and tolerance; immune system changes during pregnancy are partly explained by hormonal changes; pregnant women with asthma have higher levels of proinflammatory chemokines and higher oxidative stress throughout the pregnancy#

$PaCO_2$ = ; FVC = forced vital capacity; FEV_1, = forced expiratory volume in the first second of expiration; PEF = peak expiratory flow; $PaCO_2$ = partial pressure of carbon dioxide.
**From Ref. 12.*
#Adapted from Ref. 92.

during the first and second trimesters.[12–14] Importantly, compared with pregnant women who are not asthmatic, lung function changes are more pronounced in pregnant women with asthma.

The immune system also changes during pregnancy. For instance, there is a predominant T-helper type 1 (Th1) response in the first trimester with a subsequent shift to a T-helper type 2 (Th2) response in the second and third trimesters.[15,16] The recruitment of specialized immune cells occurs within the decidua on implantation, which mostly contains macrophages, natural killer cells, regulatory T cells (Treg), and dendritic cells, which creates a proinflammatory environment that favors trophoblastic invasion.[17,18] After the first weeks of gestation, there are changes in B-cell populations, including a decrease in total B-cell numbers.[18,19] Among the most significant changes, an increasing regulatory B cell population promotes immune tolerance to avoid fetal rejection.[20] Furthermore, there is evidence that Tregs also promote anti-inflammatory conditions during the second trimester.[21] Interestingly, other studies[22–44] have shown multiple abnormalities in immune cell subgroups of women with asthma during pregnancy. There is an increased number of B cells, memory cells, plasmablasts,[22] monocytes, and neutrophils compared with women who are not asthmatic.[23] In addition, the pregnancy-induced increase in Tregs is decreased in asthmatic pregnancy, which may interfere with fetal development and tolerance.[24]

Hormonal changes during pregnancy also influence the cytokine milieu.[25] In particular, the gradual increase of estrogen and progesterone at the end of the first trimester reduces tumor necrosis factor α production, interferon (IFN) γ expression, and natural killer cell activity, facilitating an anti-inflammatory environment.[26] In pregnant women with asthma, an abnormally increased Th2 response is present.[26] Notably, an observational study in pregnant women found higher levels of interleukin (IL) 4, IL-6, and IFN-γ.[27] In addition, a statistically significant negative correlation has been reported between the levels of IL-4 and IFN-γ and maternal peak expiratory flow among pregnant women with asthma.[28] Furthermore, asthma during pregnancy increases the circulating level of proinflammatory C5a, which is accompanied by impaired lung function and partly counteracted by the gestation-specific elevation of regulatory complement factor H level.[29] Exhaled breath condensate pH is higher in healthy pregnant women compared with their counterparts with asthma, which suggests oxidative inflammation at play in pregnant women with asthma.[30] Moreover, studies have also shown an increase in exhaled breath condensate pH during asthma exacerbations.[31] The physiologic changes during pregnancy are summarized in Table 1.

DIAGNOSIS

Most pregnant women with asthma already have an established diagnosis before gestation. For those who present with respiratory symptoms during pregnancy and without a previous diagnosis of asthma, multiple conditions need to be considered. Importantly, 60% of pregnant women report shortness of breath due to the previously described changes in the pulmonary system.[32] However, shortness of breath that impairs functionality and the association with other symptoms such as chest pain, cough, or wheezing warrant further workup. Medical conditions to consider include upper

Table 2 **Asthma severity classification in pregnant women***

Severity	Daytime Symptoms	Nighttime Symptoms	Impaired Functionality	FEV_1 or PEF, %	PEF Variability, %
Severe persistent	Constantly	>4 times/week	Very limited	<60	>30
Moderate persistent	Frequently	>1 time/week	Limited	60–80	>30
Mild persistent	>2 times/week but not daily	>2 times/month	Minor limitation	>80	20–30
Mild intermittent	<2 days/week	<2 times/month	None	>80	<30

FEV_1, = Forced expiratory volume in the first second of expiration; PEF = peak expiratory flow.
**Adapted from Ref. 67.*

respiratory infections, gastroesophageal reflux disease, pulmonary embolism, pulmonary edema, and asthma.[33]

A clinical presentation typical of asthma increases the probability of this condition but is not confirmatory. Importantly, forced vital capacity and forced expiratory volume in the first second do not change during pregnancy.[10] A confirmed parameter of expiratory flow limitation should be met with lung function testing and a bronchodilator test, as referenced in The Working Group on Asthma and Pregnancy Guidelines.[34] In addition, asthma severity is classified according to the parameters defined by the National Asthma Education and Prevention Program Working Group on Asthma and Pregnancy as mild, moderate, moderate with additional therapy, and severe (Table 2). This classification considers daytime and nighttime symptoms plus spirometry values and implications for treatment options.[35,36]

FOLLOW-UP

Asthma's course during pregnancy is highly variable. Retrospective and prospective studies have shown that asthma worsens in a third of patients, improves in a fourth of patients, and remains unchanged in a third of them, with similar disease courses in subsequent pregnancies.[37] In addition, asthma severity during pregnancy is similar to the severity observed during the prepregnancy state when these patients continued to use their medications.[38] Determinants of low-risk asthma exacerbation are clinically stable asthma, no history of exacerbations, and no necessity of treatment with controller medication because of mild disease.[39]

Evaluation of asthma control during pregnancy is critical, and it should be assessed by spirometry and validated questionnaires in prenatal visits.[40] As described in the Global Initiative for Asthma (GINA) recommendations,[41] an assessment of asthma symptom control could be made by questioning the frequency of asthma symptoms, the necessity of short-acting inhaled therapy, and the time of appearance of such symptoms. In addition, numerical questionnaires, *e.g.*, the Asthma Control Test (QualityMetric Incorporated, Johnston), have been used and validated to assess asthma control in pregnant women.[42,43]

Other tools to assist asthma control evaluation during follow-up of pregnant patients are being studied. For instance, fractional exhaled nitric oxide (FeNO), was evaluated in a prospective study[44] in which 111 women were randomly assigned to the FeNO group. An exacerbation rate was lower in the FeNO group than in the control group, with a number needed to treat of six. In the FeNO group, the quality of life was improved.[44,45] As with nonpregnant adults with asthma, further studies are needed to evaluate FeNO-guided treatment.

MATERNAL AND FETAL OUTCOMES

Asthma has been associated with a wide variety of complications and adverse outcomes for mothers in all phases of gestation and among neonates, with a growing prevalence in recent years.[46] As stated by Kwon *et al.*,[47] higher numbers of pregnant women with asthma are driven by an increasing prevalence of asthma among younger pregnant women, likely as a consequence of lifestyle and urbanization changes.[48,49] Some investigators postulate that complications among pregnant women are increasing due to increased obesity, consumption of tobacco products, and a higher prevalence of psychosocial issues.[50] Some complications reported by observational studies include spontaneous abortion, antepartum and postpartum hemorrhage, placental abruption, gestational diabetes, cesarean section, placenta previa, premature rupture of membranes, preterm birth, a higher risk of a breech presentation, pulmonary embolism, and maternal intensive care unit admission.[51–56]

Furthermore, it seems that asthma severity influences the risk of complications because adverse outcomes are more prevalent in pregnant women with moderate-to-severe asthma.[52] Pregnant women with asthma are also at an increased risk of experiencing transient hypertension of pregnancy, preeclampsia, or eclampsia.[57] Notably, obesity and weight gain during pregnancy have also been associated with worse outcomes in

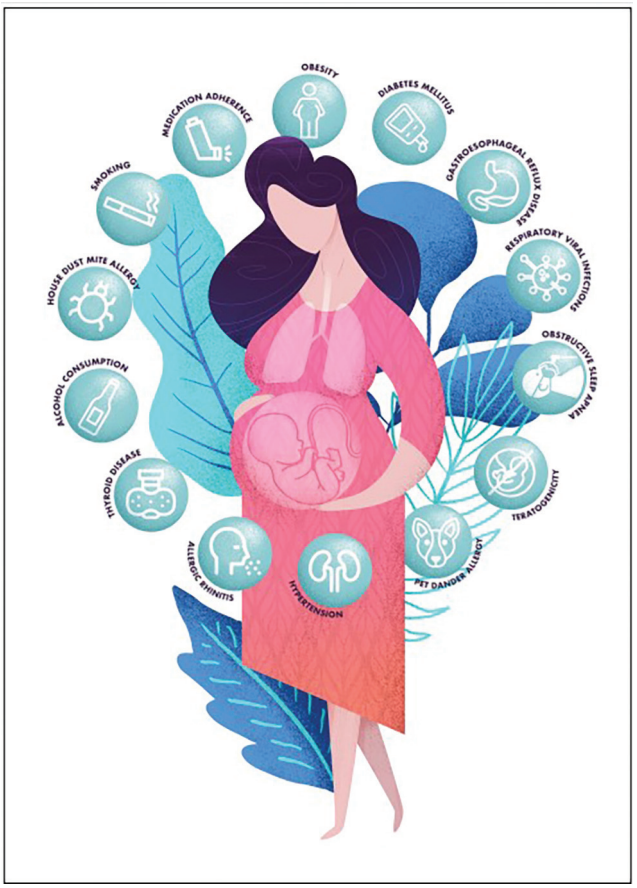

Figure 1. *Comorbidities and socioeconomical factors to consider when managing women with asthma during pregnancy.*

pregnant patients with asthma, and this relationship seems to increase in a dose-dependent matter.[58] Maternal asthma is also associated with an increased risk of multiple diseases in the offspring, including infectious, respiratory, cutaneous, and hematologic illnesses,[59] and childhood asthma.[60] A higher rate of congenital abnormalities and being small for gestational age have also been noted.[46] In contrast, another study found no significant association between maternal asthma and birth weight, Apgar scores, or respiratory distress syndrome.[61]

TREATMENT

Management of asthma in pregnant patients includes education about the disease, inhaler technique, the importance of adherence independent of risk classification, and management of other associated comorbidities.[62] It is essential to identify potential roadblocks to adequate asthma management in pregnant women (Fig. 1). A retrospective cohort study of 115,169 pregnant women with asthma recognized a tendency of these patients to decrease their asthma therapy during gestation with a subsequent increase in the rate of exacerbations.[63] Furthermore, poor asthma control was observed in pregnant women with lower income, less education, younger age, and a smoking habit.[64,65] Clinicians need to adequately assess concerns about asthma management and perceptions of disease course to ensure proper adherence.[66]

Pregnant women with asthma and with associated comorbidities, including atopy, rhinitis, and gastroesophageal reflux disease, require proper management to avoid poor asthma control (Table 3). For instance, atopy treatment needs lifestyle modifications and avoidance of common allergens, including pet dander, pollens, mold, house-dust mite, and cockroaches,[67] to decrease the probability of asthma exacerbations.[68] Allergen-specific immunotherapy may be continued if started before conception, but its initiation is contraindicated during pregnancy due to concerns of anaphylaxis.[69]

Multiple studies exhibited the association of appropriate asthma control and perception of the disease with multidisciplinary team involvement in the care of pregnant women with asthma.[70] Interestingly, antenatal asthma management services reduce the risk of exacerbations, persistent uncontrolled asthma, and loss of disease control.[58,71,72] In this regard, a randomized control trial that involved 60 pregnant women with asthma evaluated a multidisciplinary model of care for asthma management, including monitoring, education, and pharmacist-led intervention.[73] This study demonstrated a decrease in the rate of asthma exacerbations and improvement in disease control among pregnant women.[73]

As mentioned in the GINA recommendations,[41] asthma management should consider symptom control and risk reduction when prescribing medication. There is evidence of the importance of controlling asthma exacerbations in pregnant women to avoid substantial morbidity, mortality, and adverse fetal outcomes.[74,75] As such, continuing inhaled therapy during pregnancy outweighs the risks of potential medication adverse effects.[76,77] Medications for pregnant women with asthma include inhaled corticosteroids, leukotriene receptor antagonists, long-acting β_2-agonists, short-acting β_2-agonists, inhaled muscarinic antagonists, and, most recently, biologics.[41] The therapeutic options according to asthma severity are summarized in Table 4.[41]

Medication nonadherence is a critical problem when managing pregnant women with asthma. In a population-based control study[78] that describes the use of asthma medications during pregnancy, the investigators described that 85% of women with asthma used albuterol, 46% used fluticasone, and 15% used montelukast. Importantly, 70% of women who used inhaled bronchodilators during the preconception period continued their use amid gestation,[78] with other medications being more frequently discontinued.[79] Limitations

Table 3 **Comorbidities that can exacerbate asthma during pregnancy**

Comorbidity and References	Comment and References
GERD[90,93,94]	Prevalence was high in pregnant women in general[93]; increased relaxation of the lower esophageal sphincter caused by progesterone during pregnancy exacerbates GERD and, subsequently, may increase asthma severity[90]
Respiratory viral infection[95]	Reduced antiviral interferons and increased levels of inflammatory cytokines, *e.g.*, IL-17, during pregnancy increase susceptibility, morbidity, and mortality[96,97]; also, viral infections are the most common cause of asthma exacerbations in pregnancy[98]
Diabetes mellitus[46,99]	Poorly controlled diabetes is associated with increased asthma exacerbations[100]; also, associated with wheezing in the child of mother with diabetes[101–103]
Chronic arterial hypertension[46]	Asthma increases the likelihood of hypertensive disorders of pregnancy, including chronic arterial hypertension, which, in turn, increases the probability of wheezing in offspring[104]
Obstructive sleep apnea[105]	Increases the risk of severe asthma[106]
Obesity[107]	Obesity during pregnancy increases the likelihood of asthma in offspring[108,109]
Thyroid disease[46]	Maternal hypothyroidism increases the probability of childhood wheezing[110]
Smoking[46]	Asthma severity is correlated with smoking[111]; maternal cigarette consumption is associated with asthma in the offspring[112]
Alcohol consumption[113]	Increased alcohol consumption is associated with asthma severity and exacerbations[113]
Illicit drug use[114]	Associated with socioeconomic and race disparities[114]
Allergic rhinitis[115]	Correlation between asthma and allergy control with severe asthma has been observed[115,116]
Rhinitis during pregnancy[117–119]	Increased cholinergic activity caused by estrogen during pregnancy results in nasal mucosa edema, rhinorrhea, and congestion[117]; arises in ~20% of pregnancies[120]
Fertility[121]	Thought to be secondary to increased inflammation within the decidua, which impairs implantation[122]; also associated with a prolonged time to conception[123]
Psychiatric comorbidities, such as depression and anxiety disorders[124]	Associated with increased asthma exacerbations[125]; asthma in pregnancy is correlated with postpartum depression[126]

GERD = Gastroesophageal reflux disease; IL = interleukin.

for adequate asthma management include medication safety concerns during pregnancy because women perceive a deleterious effect on the fetus as a reason to discontinue therapy. Importantly, evidence from multiple observational studies has not shown a statistically significant correlation between inhaled therapy and congenital heart defects,[78] and cleft lip, stillbirth, neonatal hospitalization, respiratory distress syndrome, and neonatal sepsis.[80] Notably, inhaled corticosteroids do not seem to affect fetal adrenal function.[81]

It is also important to note that there is a surge in novel therapies for asthma, including biologics, *e.g.*, omalizumab.[70] Notably, a prospective cohort study did not demonstrate an increased risk of congenital abnormalities in pregnant women treated with omalizumab.[70] Nonetheless, because evidence is limited, current guidelines recommend continuing the use of omalizumab in pregnant women treated preconceptionally and not initiating it during pregnancy.[82] Animal studies and case reports of patients with asthma who received anti–IL-5 biologics and dupilumab during pregnancy suggest that these biologics have a good safety profile.[83–89] Further prospective studies are warranted to investigate the effects of asthma biologics during pregnancy.

Experimental and epidemiologic evidence has revealed increased reactive oxygen species production and inflammation during asthma in pregnancy. Introducing dietary antioxidants might decrease asthma severity,[90] as demonstrated in some randomized controlled trials that used lycopene and β-carotene as supplements.[91,92] However, interventional studies in pregnant women with asthma are needed to fully elucidate the benefits of antioxidants in this population.[62]

Table 4 **Medications for the management of asthma during pregnancy**

Medication	Comment and References
ICS	A pillar of asthma management as a controller and reliever when combined with formoterol in mild intermittent asthma; combined with another LABA in mild persistent, moderate persistent, and severe persistent asthma, with dose increments, depending on severity; overall, evidence has shown safety with the use of ICS [63,76,78,113,127–129]; evidence has not shown an increased risk of congenital heart defects,[76] preterm birth, low birth weight,[130] or other congenital malformations[129]
LABA	Used as a controller in combination with ICS in patients with moderate persistent and severe persistent asthma; evidence in animal experiments and observational studies in humans have shown safety with formoterol and salmeterol[131]
LRA	Used as a second-line controller in mild persistent asthma and in combination with ICS in moderate persistent asthma; limited evidence has shown safety with montelukast and zafirlukast[62,68,127,132–134]
Anti-IgE	Omalizumab is used as an add-on in moderate-to-severe persistent asthma, despite appropriate use of ICS; there is limited evidence of safety with omalizumab, with a prospective observational exposure registry study of 250 pregnant women with asthma who used omalizumab, with no evidence of congenital anomalies[80]; nonetheless, omalizumab should not be initiated during pregnancy[135]
Anti–IL-5	Anti–IL-5 medications are indicated as an add-on maintenance therapy in persons with severe eosinophilic asthma,[136] and most cross the placenta during the third trimester[137]; pregnant monkeys exposed to benralizumab did not encounter fetal malformations or limited neonatal growth[137]; fetal harm was not evidenced in animal studies that used mepolizumab; there are few case reports of pregnant women exposed to mepolizumab without fetal outcomes assessed[138,139]; no evidence of fetal malformations was shown in studies of animals while they were exposed to reslizumab; no human studies exist[140]
Anti–IL-4 and -13	Dupilumab is indicated as add-on therapy for severe eosinophilic asthma or oral corticosteroid–dependent asthma[141]; no evidence of fetal adverse outcomes was noted in pregnant monkeys exposed to dupilumab; no human studies[128,140]
SABA	Used as a second-line inhaler for symptom relief; limited observational studies showed safety with albuterol and formoterol[131]; formoterol is used as a symptom reliever in combination with an ICS[41]
Systemic corticosteroids	Used in acute asthma exacerbations and severe asthma; despite concerns of congenital anomalies, such as cleft palate,[142] preterm birth, and low birth weight, [130,143–145] the benefits of using oral corticosteroids when indicated outweigh these risks; other obstetric complications related to oral corticosteroids include preeclampsia[146]
Inhaled muscarinic antagonists	Used as add-on in acute exacerbations and moderate-to-severe uncontrolled asthma, despite LABA-ICS therapy; high doses of tiotropium bromide may induce fetal toxicity in animal studies; no evidence in humans exists[128]; evidence when using ipratropium bromide indicates no fetal harm in animal studies at high doses[147]

ICS = Inhaled corticosteroid; LABA = long-acting β-2 agonist; LRA = leukotriene receptor antagonist; IgE = immunoglobulin E; IL = interleukin; SABA = short-acting β2-agonists.

MANAGEMENT OF ACUTE EXACERBATIONS

Fifty percent of asthma exacerbations during pregnancy occur before 20 weeks of gestation [93] and are associated with adverse obstetric outcomes,[94] including congenital malformations when severe exacerbations occur during the first trimester,[95] low birth weight,[93] preterm delivery,[96] preeclampsia, and spontaneous abortion.[97] Overall, treatment of asthma exacerbations during pregnancy is similar to patients who are not pregnant. First, exacerbation severity should be assessed by measuring expiratory airflow with a peak flow meter. Constant maternal and fetal monitoring must be ensured by using maternal oxygen saturation >95% and fetal heart rate testing; signs of impending respiratory failure must be routinely evaluated.

Special consideration to physiologic changes in the acid-base balance during pregnancy is required when interpreting arterial blood gas results because an apparent normal partial pressure of carbon dioxide ($PaCO_2$) may signify a more severe respiratory compromise.[69] Medications should include supplemental oxygen titrated to maintain adequate saturation, short-acting β-agonists, inhaled muscarinic antagonists (*e.g.,* ipratropium bromide), systemic glucocorticoids in oral or intravenous preparations, and adjunct therapies in poor response, including magnesium sulfate and terbutaline.[67,69]

PERIPARTUM MANAGEMENT OF ASTHMA

Pregnant patients with asthma have a higher incidence of labor induction with oxytocin and cesarean section rates.[98] Furthermore, ~10% of pregnant patients with asthma will have increased symptoms during labor, usually controlled with bronchodilators.[99] During labor and delivery, asthma therapy should be continued and adequate hydration and analgesia must be provided to avoid complications.[35] Generally, labor and delivery management medications are safe with a few exceptions; among them, the prostaglandin F2-α analogs (*e.g.,* carboprost) cause bronchoconstriction in animal studies and are contraindicated in pregnant women with asthma.[100] Also, the use of morphine and meperidine for pain control should be avoided due to the risk of inducing histamine release.[67]

CONCLUSION

Further studies are required to elucidate the pathologic mechanisms involved in pregnant women with asthma. Moreover, additional investigations of the variable behaviors of asthma during gestation and the determinants that influence asthma's severity during pregnancy are warranted. Future directions should also focus on determining the risks of adverse maternal and fetal outcomes associated with specific asthma medications. This is particularly important given the advent of novel biologics for the treatment of asthma.

REFERENCES

1. Cohen JM, Bateman BT, Huybrechts KF, et al. Poorly controlled asthma during pregnancy remains common in the United States. J Allergy Clin Immunol Pract. 2019; 7:2672–2680.e10.
2. Ceulemans M, Lupattelli A, Nordeng H, et al. Women's beliefs about medicines and adherence to pharmacotherapy in pregnancy: opportunities for community pharmacists. Curr Pharm Des. 2019; 25:469–482.
3. Baarnes CB, Hansen AV, Ulrik CS. Enrolment in an asthma management program during pregnancy and adherence with inhaled corticosteroids: the 'Management of Asthma during Pregnancy' Program. Respiration. 2016; 92:9–15.
4. Mahendru AA, Everett TR, Wilkinson IB, et al. A longitudinal study of maternal cardiovascular function from preconception to the postpartum period. J Hypertens. 2014; 32:849–856.
5. Bader RA, Bader ME, Rose DF, et al. Hemodynamics at rest and during exercise in normal pregnancy as studies by cardiac catheterization. J Clin Invest. 1955; 34:1524–1536.
6. Nelson-Piercy C, Waldron M, Moore-Gillon J. Respiratory disease in pregnancy. Br J Hosp Med. 1994; 51:398–401.
7. Pereira A, Krieger BP. Pulmonary complications of pregnancy. Clin Chest Med. 2004; 25:299–310.
8. Crapo RO. Normal cardiopulmonary physiology during pregnancy. Clin Obstet Gynecol. 1996; 39:3–16.
9. Vatti RR, Teuber SS. Asthma and pregnancy. Clin Rev Allergy Immunol. 2012; 43:45–56.
10. Grindheim G, Toska K, Estensen M-E, et al. Changes in pulmonary function during pregnancy: a longitudinal cohort study. BJOG. 2012; 119:94–101.
11. Zairina E, Abramson MJ, McDonald CF, et al. A prospective cohort study of pulmonary function during pregnancy in women with and without asthma. J Asthma. 2016; 53:155–163.
12. Prowse CM, Gaensler EA. Respiratory and acid-base changes during pregnancy. Anesthesiology. 1965; 26:381–392.
13. Tenholder MF, South-Paul JE. Dyspnea in pregnancy. Chest. 1989; 96:381–388.
14. Simon PM, Schwartzstein RM, Weiss JW, et al. Distinguishable types of dyspnea in patients with shortness of breath. Am Rev Respir Dis. 1990; 142:1009–1014.
15. Aris A, Lambert F, Bessette P, et al. Maternal circulating interferon-gamma and interleukin-6 as biomarkers of Th1/Th2 immune status throughout pregnancy. J Obstet Gynaecol Res. 2008; 34:7–11.
16. Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. Am J Reprod Immunol. 2010; 63:425–433.
17. Hanna J, Goldman-Wohl D, Hamani Y, et al. Decidual NK cells regulate key developmental processes at the human fetal-maternal interface. Nat Med. 2006; 12:1065–1074.
18. Bulmer JN, Pace D, Ritson A. Immunoregulatory cells in human decidua: morphology, immunohistochemistry and function. Reprod Nutr Dev. 1988; 28:1599–1613.
19. Dutta S, Sengupta P, Haque N. Reproductive immunomodulatory functions of B cells in pregnancy. Int Rev Immunol. 2020; 39:53–66.
20. Guzman-Genuino RM, Diener KR. Regulatory B cells in pregnancy: lessons from autoimmunity, graft tolerance, and cancer. Front Immunol. 2017; 8:172.
21. Mor G, Aldo P, Alvero AB. The unique immunological and microbial aspects of pregnancy. Nat Rev Immunol. 2017; 17:469–482.
22. Martins C, Lima J, Nunes G, et al. Pregnancy alters the circulating B cell compartment in atopic asthmatic women, and

transitional B cells are positively associated with the development of allergy manifestations in their progeny. Am J Reprod Immunol. 2016; 76:465–474.
23. Osei-Kumah A, Wark PAB, Smith R, et al. Asthma during pregnancy alters immune cell profile and airway epithelial chemokine release. Inflamm Res. 2010; 59:349–358.
24. Bohács A, Cseh A, Stenczer B, et al. Effector and regulatory lymphocytes in asthmatic pregnant women. Am J Reprod Immunol. 2010; 64:393–401.
25. Piccinni M-P, Raghupathy R, Saito S, et al. Cytokines, hormones and cellular regulatory mechanisms favoring successful reproduction. Front Immunol. 2021; 12:717808.
26. Baldaçara RP, Silva I. Association between asthma and female sex hormones. Sao Paulo Med J. 2017; 135:4–14.
27. Osei-Kumah A, Ammit AJ, Smith R, et al. Inflammatory mediator release in normal bronchial smooth muscle cells is altered by pregnant maternal and fetal plasma independent of asthma. Placenta. 2006; 27:847–852.
28. Tamási L, Bohács A, Pállinger E, et al. Increased interferon-gamma- and interleukin-4-synthesizing subsets of circulating T lymphocytes in pregnant asthmatics. Clin Exp Allergy. 2005; 35:1197–1203.
29. Bohács A, Bikov A, Ivancsó I, et al. Relationship of circulating C5a and complement factor H levels with disease control in pregnant women with asthma. Respir Care. 2016; 61:502–509.
30. Eszes N, Bikov A, Lázár Z, et al. Changes in exhaled breath condensate pH in healthy and asthmatic pregnant women. Acta Obstet Gynecol Scand. 2013; 92:591–597.
31. Caffarelli C, Dascola CP, Peroni D, et al. Airway acidification in childhood asthma exacerbations. Allergy Asthma Proc. 2014; 35:51–56.
32. Jensen D, Webb KA, Davies GA, et al. Mechanisms of activity-related breathlessness in healthy human pregnancy. Eur J Appl Physiol. 2009; 106:253–265.
33. Bidad K, Heidarnazhad H, Pourpak Z, et al. Frequency of asthma as the cause of dyspnea in pregnancy. Int J Gynaecol Obstet. 2010; 111:140–143.
34. Stone RG, McDonald M, Elnazir B. Global Initiative for Asthma 2019 Guidelines: new changes to the treatment of mild asthmatics 12 years and older. Ir Med J. 2020; 113:69.
35. Dombrowski MP, Schatz M, ACOG Committee on Practice Bulletins-Obstetrics. ACOG practice bulletin: clinical management guidelines for obstetrician-gynecologists number 90, February 2008: asthma in pregnancy. Obstet Gynecol. 2008; 111(pt 1):457–464.
36. Luskin AT. An overview of the recommendations of the Working Group on Asthma and Pregnancy. National Asthma Education and Prevention Program. J Allergy Clin Immunol. 1999; 103 (pt 1):S350–S353.
37. Schatz M, Harden K, Forsythe A, et al. The course of asthma during pregnancy, post partum, and with successive pregnancies: a prospective analysis. J Allergy Clin Immunol. 1988; 81:509–517.
38. Belanger K, Hellenbrand ME, Holford TR, et al. Effect of pregnancy on maternal asthma symptoms and medication use. Obstet Gynecol. 2010; 115:559–567.
39. Ali Z, Nilas L, Ulrik CS. Determinants of low risk of asthma exacerbation during pregnancy. Clin Exp Allergy. 2018; 48:23–28.
40. Amaral L, Martins C, Coimbra A. Use of the Control of Allergic Rhinitis and Asthma Test and pulmonary function tests to assess asthma control in pregnancy. Aust N Z J Obstet Gynaecol. 2018; 58:86–90.
41. Global Strategy for Asthma Management and Prevention. 2020. Available online at www.ginasthma.org; accessed January 12, 2022.
42. Schatz M, Sorkness CA, Li JT, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. J Allergy Clin Immunol. 2006; 117:549–556.
43. Palmsten K, Schatz M, Chan PH, et al. Validation of the Pregnancy Asthma Control Test. J Allergy Clin Immunol Pract. 2016; 4:310–315.e1.
44. Powell H, Murphy VE, Taylor DR, et al. Management of asthma in pregnancy guided by measurement of fraction of exhaled nitric oxide: a double-blind, randomised controlled trial. Lancet. 2011; 378:983–990.
45. Tamási L, Bohács A, Bikov A, et al. Exhaled nitric oxide in pregnant healthy and asthmatic women. J Asthma. 2009; 46:786–791.
46. Baghlaf H, Spence AR, Czuzoj-Shulman N, et al. Pregnancy outcomes among women with asthma. J Matern Fetal Neonatal Med. 2019; 32:1325–1331.
47. Kwon HL, Belanger K, Bracken MB. Asthma prevalence among pregnant and childbearing-aged women in the United States: estimates from national health surveys. Ann Epidemiol. 2003; 13:317–324.
48. Lundback B, Backman H, Lotvall J, et al. Is asthma prevalence still increasing? Expert Rev Respir Med. 2016; 10:39–51.
49. Backman H, Raisanen P, Hedman L, et al. Increased prevalence of allergic asthma from 1996 to 2006 and further to 2016—results from three population surveys. Clin Exp Allergy. 2017; 47:1426–1435.
50. Carter RM, Symons Downs D, Bascom R, et al. The moderating influence of asthma diagnosis on biobehavioral health characteristics of women of reproductive age. Matern Child Health J. 2012; 16:448–455.
51. Blais L, Kettani F-Z, Forget A. Relationship between maternal asthma, its severity and control and abortion. Hum Reprod. 2013; 28:908–915.
52. Wang G, Murphy VE, Namazy J, et al. The risk of maternal and placental complications in pregnant women with asthma: a systematic review and meta-analysis. J Matern Fetal Neonatal Med. 2014; 27:934–942.
53. Mendola P, Laughon SK, Männistö TI, et al. Obstetric complications among US women with asthma. Am J Obstet Gynecol. 2013; 208:127.e1-8.
54. Firoozi F, Lemiere C, Beauchesne M-F, et al. Impact of maternal asthma on perinatal outcomes: a two-stage sampling cohort study. Eur J Epidemiol. 2012; 27:205–214.
55. Kemppainen M, Lahesmaa-Korpinen A-M, Kauppi P, et al. Maternal asthma is associated with increased risk of perinatal mortality. PLoS One. 2018; 13:e0197593.
56. Vaezi A, Haghighi L, Beigmohammadi F, et al. Maternal asthma, pregnancy, delivery and birth outcomes: a retrospective cohort study. Iran J Allergy Asthma Immunol. 2017; 16:92–98.
57. Wang M, He W, Li M, et al. Maternal asthma and the risk of hypertensive disorders of pregnancy: a systematic review and meta-analysis of cohort studies. Hypertens Pregnancy. 2020; 39:12–24.
58. Ali Z, Nilas L, Ulrik CS. Excessive gestational weight gain in first trimester is a risk factor for exacerbation of asthma during pregnancy: a prospective study of 1283 pregnancies. J Allergy Clin Immunol. 2018; 141:761–767.
59. Tegethoff M, Olsen J, Schaffner E, et al. Asthma during pregnancy and clinical outcomes in offspring: a national cohort study. Pediatrics. 2013; 132:483–491.
60. Venter C, Palumbo MP, Sauder KA, et al. Incidence and timing of offspring asthma, wheeze, allergic rhinitis, atopic dermatitis, and food allergy and association with maternal history of asthma and allergic rhinitis. World Allergy Organ J. 2021; 14:100526.

61. Fazel N, Kundi M, Jensen-Jarolim E, et al. Prospective cohort study of pregnancy complications and birth outcomes in women with asthma. Arch Gynecol Obstet. 2018; 298:279–287.
62. Murphy VE. Managing asthma in pregnancy. Breathe (Sheff). 2015; 11:258–267.
63. Koo S-M, Kim Y, Park C, et al. Effect of pregnancy on quantitative medication use and relation to exacerbations in asthma. Biomed Res Int. 2017; 2017:8276190.
64. Louik C, Schatz M, Hernández-Díaz S, et al. Asthma in pregnancy and its pharmacologic treatment. Ann Allergy Asthma Immunol. 2010; 105:110–117.
65. Zetstra-van der Woude PA, Vroegop JS, Bos HJ, et al. A population analysis of prescriptions for asthma medications during pregnancy. J Allergy Clin Immunol. 2013; 131:711–717.
66. Lim AS, Stewart K, Abramson MJ, et al. Asthma during pregnancy: the experiences, concerns and views of pregnant women with asthma. J Asthma. 2012; 49:474–479.
67. National Heart, Lung, and Blood Institute, National Asthma Education and Prevention Program Asthma and Pregnancy Working Group. NAEPP expert panel report. Managing asthma during pregnancy: recommendations for pharmacologic treatment-2004 update. J Allergy Clin Immunol. 2005; 115:34–46.
68. Sande AK, Torkildsen EA, Sande RK, et al. Maternal allergy as an isolated risk factor for early-onset preeclampsia: an epidemiological study. J Reprod Immunol. 2018; 127:43–47.
69. Bonham CA, Patterson KC, Strek ME. Asthma outcomes and management during pregnancy. Chest. 2018; 153:515–527.
70. Mihălţan FD, Antoniu SA, Ulmeanu R. Asthma and pregnancy: therapeutic challenges. Arch Gynecol Obstet. 2014; 290:621–627.
71. Grzeskowiak LE, Smith B, Roy A, et al. An observational study of the impact of an antenatal asthma management service on asthma control during pregnancy. Eur J Obstet Gynecol Reprod Biol. 2016; 197:48–53.
72. Ibrahim WH, Rasul F, Ahmad M, et al. Asthma knowledge, care, and outcome during pregnancy: the QAKCOP study. Chron Respir Dis. 2019; 16:1479972318767719.
73. Lim AS, Stewart K, Abramson MJ, et al. Multidisciplinary Approach to Management of Maternal Asthma (MAMMA): a randomized controlled trial. Chest. 2014; 145:1046–1054.
74. Murphy VE, Namazy JA, Powell H, et al. A meta-analysis of adverse perinatal outcomes in women with asthma. BJOG. 2011; 118:1314–1323.
75. Rejnö G, Lundholm C, Larsson K, et al. Adverse pregnancy outcomes in asthmatic women: a population-based family design study. J Allergy Clin Immunol Pract. 2018; 6:916–922.e6.
76. Schatz M, Dombrowski MP, Wise R, et al. The relationship of asthma-specific quality of life during pregnancy to subsequent asthma and perinatal morbidity. J Asthma. 2010; 47:46–50.
77. Shaked E, Wainstock T, Sheiner E, et al. Maternal asthma: pregnancy course and outcome. J Matern Fetal Neonatal Med. 2019; 32:103–108.
78. Van Zutphen AR, Bell EM, Browne ML, et al. Maternal asthma medication use during pregnancy and risk of congenital heart defects. Birth Defects Res A Clin Mol Teratol. 2015; 103:951–961.
79. Chambers K. Asthma education and outcomes for women of childbearing age. Case Manager. 2003; 14:58–61.
80. Murphy VE, Wang G, Namazy JA, et al. The risk of congenital malformations, perinatal mortality and neonatal hospitalisation among pregnant women with asthma: a systematic review and meta-analysis. BJOG. 2013; 120:812–822.
81. Hodyl NA, Stark MJ, Osei-Kumah A, et al. Fetal glucocorticoid-regulated pathways are not affected by inhaled corticosteroid use for asthma during pregnancy. Am J Respir Crit Care Med. 2011; 183:716–722.
82. Namazy JA, Blais L, Andrews EB, et al. Pregnancy outcomes in the omalizumab pregnancy registry and a disease-matched comparator cohort. J Allergy Clin Immunol. 2020; 145:528–536.e1.
83. Kage P, Simon J-C, Treudler R. Case of atopic eczema treated with dupilumab throughout conception, pregnancy, and lactation. J Dermatol. 2021; 48:E484–E485.
84. Lobo Y, Lee RC, Spelman L. Atopic dermatitis treated safely with dupilumab during pregnancy: a case report and review of the literature. Case Rep Dermatol. 2021; 13:248–256.
85. Mian M, Dunlap R, Simpson E. Dupilumab for the treatment of severe atopic dermatitis in a pregnant patient: a case report. JAAD Case Rep. 2020; 6:1051–1052.
86. Gracia-Darder I, Pons De Ves J, Reyero Cortina M, et al. Patient with atopic dermatitis, hyper IgE syndrome and ulcerative colitis, treated successfully with dupilumab during pregnancy. Dermatol Ther. 2022; 35:e15237.
87. Costley M, Murphy B. Severe atopic dermatitis treated successfully with dupilumab throughout pregnancy. Clin Exp Dermatol. 2022; 47:960–961.
88. Riquelme-Mc Loughlin C, Mascaro JM Jr. Treatment of pemphigoid gestationis with dupilumab. Clin Exp Dermatol. 2021; 46:1578–1579.
89. Akhtar NH, Khosravi-Hafshejani T, Akhtar D, et al. The use of dupilumab in severe atopic dermatitis during pregnancy: a case report. Allergy Asthma Clin Immunol. 2022; 18:9.
90. Grieger JA, Wood LG, Clifton VL. Improving asthma during pregnancy with dietary antioxidants: the current evidence. Nutrients. 2013; 5:3212–3234.
91. Wood LG, Garg ML, Powell H, et al. Lycopene-rich treatments modify noneosinophilic airway inflammation in asthma: proof of concept. Free Radic Res. 2008; 42:94–102.
92. Neuman I, Nahum H, Ben-Amotz A. Prevention of exercise-induced asthma by a natural isomer mixture of beta-carotene. Ann Allergy Asthma Immunol. 1999; 82:549–553.
93. Grzeskowiak LE, Smith B, Roy A, et al. Patterns, predictors and outcomes of asthma control and exacerbations during pregnancy: a prospective cohort study. ERJ Open Res. 2016; 2:00054-2015.
94. Ali Z, Hansen AV, Ulrik CS. Exacerbations of asthma during pregnancy: impact on pregnancy complications and outcome. J Obstet Gynaecol. 2016; 36:455–461.
95. Blais L, Kettani F-Z, Forget A, et al. Asthma exacerbations during the first trimester of pregnancy and congenital malformations: revisiting the association in a large representative cohort. Thorax. 2015; 70:647–652.
96. Namazy JA, Murphy VE, Powell H, et al. Effects of asthma severity, exacerbations and oral corticosteroids on perinatal outcomes. Eur Respir J. 2013; 41:1082–1090.
97. Bokern MP, Robijn AL, Jensen ME, et al. Factors associated with asthma exacerbations during pregnancy. J Allergy Clin Immunol Pract. 2021; 9:4343–4352.e4.
98. Minerbi-Codish I, Fraser D, Avnun L, et al. Influence of asthma in pregnancy on labor and the newborn. Respiration. 1998; 65:130–135.
99. Gluck JC. The change of asthma course during pregnancy. Clin Rev Allergy Immunol. 2004; 26:171–180.
100. Kawikova I, Barnes PJ, Takahashi T, et al. 8-Epi-PGF2 alpha, a novel noncyclooxygenase-derived prostaglandin, constricts airways in vitro. Am J Respir Crit Care Med. 1996; 153:590–596.
101. Clifton VL, Vanderlelie J, Perkins AV. Increased anti-oxidant enzyme activity and biological oxidation in placentae of pregnancies complicated by maternal asthma. Placenta. 2005; 26:773–779.
102. Bidad K, Heidarnazhad H, Pourpak Z, et al. Gastroesophagial reflux disease and asthma in pregnant women with dyspnea. Iran J Allergy Asthma Immunol. 2014; 13:104–109.

103. Trigueros JA, Plaza V, Dominguez-Ortega J, et al. Asthma, comorbidities, and aggravating circumstances: the GEMA-FORUM II Task Force. J Investig Allergol Clin Immunol. 2020; 30:140–143.
104. Forbes RL, Gibson PG, Murphy VE, et al. Impaired type I and III interferon response to rhinovirus infection during pregnancy and asthma. Thorax. 2012; 67:209–214.
105. Vanders RL, Gibson PG, Wark PA, et al. Alterations in inflammatory, antiviral and regulatory cytokine responses in peripheral blood mononuclear cells from pregnant women with asthma. Respirology. 2013; 18:827–833.
106. Murphy VE, Powell H, Wark PAB, et al. A prospective study of respiratory viral infection in pregnant women with and without asthma. Chest. 2013; 144:420–427.
107. Murphy VE, Mattes J, Powell H, et al. Respiratory viral infections in pregnant women with asthma are associated with wheezing in the first 12 months of life. Pediatr Allergy Immunol. 2014; 25:151–158.
108. Baribeau V, Beauchesne M-F, Rey E, et al. The use of asthma controller medications during pregnancy and the risk of gestational diabetes. J Allergy Clin Immunol. 2016; 138:1732–1733.e6.
109. Cardet JC, Bulkhi AA, Lockey RF. Nonrespiratory comorbidities in asthma. J Allergy Clin Immunol Pract. 2021; 9:3887–3897.
110. Adgent MA, Gebretsadik T, Reedus J, et al. Gestational diabetes and childhood asthma in a racially diverse US pregnancy cohort. Pediatr Allergy Immunol. 2021; 32:1190–1196.
111. Azad MB, Moyce BL, Guillemette L, et al. Diabetes in pregnancy and lung health in offspring: developmental origins of respiratory disease. Paediatr Respir Rev. 2017; 21:19–26.
112. Azad MB, Becker AB, Kozyrskyj AL. Association of maternal diabetes and child asthma. Pediatr Pulmonol. 2013; 48:545–552.
113. Wilmink FA, den Dekker HT, de Jongste JC, et al. Maternal blood pressure and hypertensive disorders during pregnancy and childhood respiratory morbidity: the Generation R Study. Eur Respir J. 2018; 52:1800378.
114. Williams MA, Gelaye B, Qiu C, et al. S. Habitual snoring and asthma comorbidity among pregnant women. J Asthma. 2011; 48:91–97.
115. Bourjeily G, Barbara N, Larson L, et al. Clinical manifestations of obstructive sleep apnoea in pregnancy: more than snoring and witnessed apnoeas. J Obstet Gynaecol. 2012; 32:434–438.
116. Murphy VE, Jensen ME, Powell H, et al. Influence of maternal body mass index and macrophage activation on asthma exacerbations in pregnancy. J Allergy Clin Immunol Pract. 2017; 5:981–987.e1.
117. Miethe S, Karsonova A, Karaulov A, et al. Obesity and asthma. J Allergy Clin Immunol. 2020; 146:685–693.
118. Godfrey KM, Reynolds RM, Prescott SL, et al. Influence of maternal obesity on the long-term health of offspring. Lancet Diabetes Endocrinol. 2017; 5:53–64.
119. Liu X, Andersen SL, Olsen J, et al. Maternal hypothyroidism in the perinatal period and childhood asthma in the offspring. Allergy. 2018; 73:932–939.
120. Murphy VE, Clifton VL, Gibson PG. The effect of cigarette smoking on asthma control during exacerbations in pregnant women. Thorax. 2010; 65:739–744.
121. Toppila-Salmi S, Luukkainen AT, Xu B, et al. Maternal smoking during pregnancy affects adult onset of asthma in offspring: a follow up from birth to age 46 years. Eur Respir J. 2020; 55:1901857.
122. Almeida MLD, Santana PA, Guimaraes AM, et al. Asthma and pregnancy: repercussions for neonates. J Bras Pneumol. 2010; 36:293–300.
123. Aly H, Nada A, Ahmad T, et al. Maternal asthma, race and low birth weight deliveries. Early Hum Dev. 2011; 87:457–460.
124. Namazy J, Schatz M. The treatment of allergic respiratory disease during pregnancy. J Investig Allergol Clin Immunol. 2016; 26:1–7; quiz 2p following 7.
125. Turkeltaub PC, Cheon J, Friedmann E, et al. The influence of asthma and/or hay fever on pregnancy: data from the 1995 National Survey of Family Growth. J Allergy Clin Immunol Pract. 2017; 5:1679–1690.
126. Lekas MD. Rhinitis during pregnancy and rhinitis medicamentosa. Otolaryngol Head Neck Surg. 1992; 107(pt 2):845–848, discussion 9.
127. Schatz M, Zeiger RS. Diagnosis and management of rhinitis during pregnancy. Allergy Proc. 1988; 9:545–554.
128. Blaiss MS, Food and Drug Administration (U.S.); ACAAI-ACOG (American College of Allergy, Asthma, and Immunology and American College of Obstetricians and Gynecologists), Acaai A. Management of rhinitis and asthma in pregnancy. Ann Allergy Asthma Immunol. 2003; 90(suppl 3):16–22.
129. Mabry RL. Rhinitis of pregnancy. South Med J. 1986; 79:965–971.
130. Gade EJ, Thomsen SF, Lindenberg S, et al. Asthma affects time to pregnancy and fertility: a register-based twin study. Eur Respir J. 2014; 43:1077–1085.
131. Grzeskowiak LE, Smithers LG, Grieger JA, et al. Asthma treatment impacts time to pregnancy: evidence from the international SCOPE study. Eur Respir J. 2018; 51:1702035.
132. Vejen Hansen A, Ali Z, Malchau SS, et al. Fertility treatment among women with asthma: a case-control study of 3689 women with live births. Eur Respir J. 2019; 53: 1800597.
133. Powell H, McCaffery K, Murphy VE, et al. Psychosocial variables are related to future exacerbation risk and perinatal outcomes in pregnant women with asthma. J Asthma. 2013; 50:383–389.
134. Grzeskowiak LE, Smith B, Roy A, et al. Impact of a history of maternal depression and anxiety on asthma control during pregnancy. J Asthma. 2017; 54:706–713.
135. Blais L, Salah Ahmed SI, Beauchesne M-F, et al. Risk of postpartum depression among women with asthma. J Allergy Clin Immunol Pract. 2019; 7:925–933.e2.
136. Namazy JA, Schatz M. Pharmacotherapy options to treat asthma during pregnancy. Expert Opin Pharmacother. 2015; 16:1783–1791.
137. Middleton PG, Gade EJ, Aguilera C, et al. ERS/TSANZ Task Force Statement on the management of reproduction and pregnancy in women with airways diseases. Eur Respir J. 2020; 55:1901208.
138. Blais L, Beauchesne M-F, Lemiere C, et al. High doses of inhaled corticosteroids during the first trimester of pregnancy and congenital malformations. J Allergy Clin Immunol. 2009; 124:1229–1234.e4.
139. Schatz M, Dombrowski MP, Wise R, et al. The relationship of asthma medication use to perinatal outcomes. J Allergy Clin Immunol. 2004; 113:1040–1045.
140. Eltonsy S, Forget A, Blais L. Beta2-agonists use during pregnancy and the risk of congenital malformations. Birth Defects Res A Clin Mol Teratol. 2011; 91:937–947.
141. Bakhireva LN, Jones KL, Schatz M, et al. Safety of leukotriene receptor antagonists in pregnancy. J Allergy Clin Immunol. 2007; 119:618–625.
142. Rocklin RE. Asthma, asthma medications and their effects on maternal/fetal outcomes during pregnancy. Reprod Toxicol. 2011; 32:189–197.
143. Sarkar M, Koren G, Kalra S, et al. Montelukast use during pregnancy: a multicentre, prospective, comparative study of infant outcomes. Eur J Clin Pharmacol. 2009; 65:1259–1264.

144. Schatz M, Krishnan JA, Chambers C. Implications of changes in U.S. Food and Drug Administration Prescribing Information Regarding the Safety and Use of Asthma Biologics During Pregnancy. Ann Am Thorac Soc. 2018; 15:1131–1136.
145. Farne HA, Wilson A, Powell C, et al. Anti-IL5 therapies for asthma. Cochrane Database Syst Rev. 2017; 9:CD010834.
146. Benralizumab (Fasenra) for severe eosinophilic asthma. JAMA. 2018; 319:1501–1502.
147. Kasuya A, Kitano S, Hoshino T, et al. Successful control of severe eosinophilic granulomatosis with polyangiitis in a pregnancy and perinatal period: a use of mepolizumab. J Dermatol. 2019; 46:e309–e311. □