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Chapter 10

ASTHMA IN PREGNANCY - IMMUNOLOGY, DIAGNOSIS, AND TREATMENT

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ABSTRACT

Asthma is one of the most common diseases that complicate pregnancy and a risk factor for several maternal and fetal complications including increased perinatal mortality. Management of asthma during pregnancy poses a special challenge for physicians, as asthma influences the outcome of pregnancy and - vice versa - pregnancy affects asthma severity with bidirectional immunological interactions. Attenuation of allergic responses can be detected in controlled asthmatic pregnant patients supporting the presence of pregnancy-induced immune tolerance. However, uncontrolled asthmatic pregnant women show significant asthma-associated immune reactions, such as diminished pregnancy specific regulatory T cell proliferation and elevation of Thelper-17 cell numbers, which may - besides other factors - influence fetal growth. Uncontrolled, symptomatic asthma increases the risk of adverse perinatal outcomes; thus adequate regular anti-asthmatic treatment resulting in optimal asthma control represents a vital need during pregnancy. The diagnosis of asthma is usually known before pregnancy, but if symptoms occur for the first time during gestation, reduced forced expiratory volume in one second (FEV1) and a 12% or greater improvement in FEV1 after inhalation of a rapid acting beta-agonist confirm the diagnosis of asthma. Testing bronchial hyperresponiveness is contraindicated during pregnancy. Therapy of asthma during pregnancy must aim to control the disease, including mitigating asthma triggers as much as possible. Asthmatic women with controlled asthma should continue taking their medications during pregnancy and maintenance therapy should be increased by one step in patients with asthma that is not controlled. Very poorly controlled asthma during

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pregnancy is treated similarly to that in nonpregnant patients. This chapter summarizes immunological changes characterizing pregnancy in asthmatic women together with the clinical implications of asthma management during pregnancy.

INTRODUCTION

Asthma is probably the most common, potentially serious medical problem that may complicate pregnancy, affecting 3.7-8.4% of all gestations [1]. Asthma influences the outcome of pregnancy and - vice versa - pregnancy affects the control level and symptoms of asthma, with partly known immunological mechanisms. Asthma represents a risk factor for several maternal and fetal complications, such as asthma exacerbations, use of oral corticosteroids, hospitalizations due to asthma attacks, preeclampsia, gestational hypertension, preterm delivery, cesarean delivery, low birth weight, intrauterine growth restriction, and fetal death [2,3,4,5,6,7]. Thus, managing asthma during pregnancy requires careful decision making, optimal physician training, and frequent patient consultations with physicians treating these patients. Adequate management of asthma and maintenance of optimal asthma control during pregnancy decrease maternal and neonatal risks [8,9].

IMMUNOLOGICAL CHANGES IN HEALTHY PREGNANCY

Healthy pregnancy affects systemic immune responses (Figure 1.). The fetus is a semi-allograft for the maternal immune system, but under normal circumstances pregnancy is characterized by a physiological immune suppression, an immunological tolerance that protects the fetus from maternal immune response against paternal antigens expressed by the fetus [10]. Decidual T lymphocytes become polarized towards the T helper (Th) 2 phenotype, synthesizing IL-4, IL-5 and IL-10; cytokines which are highly expressed within the feto-maternal interface as well as in circulating lymphocytes. The physiological materno-fetal immune response exerts an ‘immunotrophic’ effect on the conceptus [13]. If the maternal immune system responds to pregnancy with Th1 cytokines (e.g. IFN-g, TNF-a), women experience spontaneous abortion [13, 14], while such a pregnancy in mice ends in fetal resorption or growth retardation [15]. However, the uterus is not the only the site of pregnancy-induced changes in immunological responses [11]. There are systemic immune effects that may cause, for example, changes in the course of various autoimmune diseases, such as systemic lupus erythematosus or rheumatoid arthritis [16].

Regulatory T (CD4+CD25high+; Treg) cells exert an inhibition on the activation of effector T lymphocytes and natural killer (NK) cells, and suppress Th2 responses to allergen. A trimester dependent, pregnancy-induced increase in circulating Treg cell number has a key role in the maintenance of maternal tolerance to paternal antigens during pregnancy [17]. Diminished numbers of Tregs in pregnancy were associated with immunological rejection of the fetus as well as preeclampsia and low fetal birth weight [18]. Of note, the inhibitory effect of proliferating Treg cells on NK lymphocytes responsible for protection against viruses [19] contributes to increased susceptibility to viral infections (e.g. influenza) during pregnancy, as observed in the H1N1 influenza pandemic in 2009 [20].

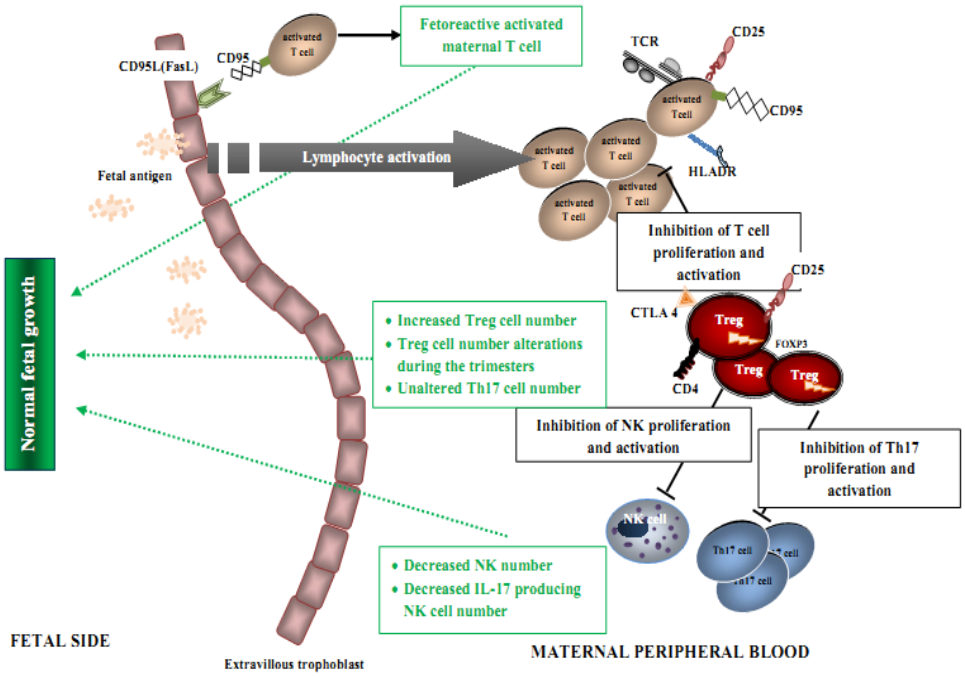

Figure 1. Cellular mechanisms of immune tolerance in healthy pregnancy (green arrows) needed for fetal well-being. Healthy pregnancy is characterized by immune tolerance mediated by trimester dependent elevation of peripheral regulatory T cell number that exerts inhibition on the activation of effector T lymphocytes and NK cells. T helper 17 prevalence remains unchanged in healthy pregnancy. (CD - cluster of differentiation; Foxp3 - fork head/winged-helix transcription factor box p3; L – ligand; TCR – T cell receptor; CTLA – cytotoxic T lymphocyte-associated antigen; HLA – human leukocyte antigen; Treg – regulatory T; NK – natural killer; Th - T helper; → stimulation; ┤ inhibition).

There are several other immunological changes associated with normal gestation, that promote the shift towards an immune tolerance, e.g. higher levels of HLA-DR+, CD11b+CD4+ and CD8+ lymphocytes [21]. Recently, the discovery of a distinct T helper subset, referred to as Th17 cells based on their IL-17 production, led to the transformation of the Th1/Th2 paradigm of immunity into a novel viewpoint that incorporates Th1, Th2, Th17 and Treg cells as elements of a complex and mutually interacting network [22]. Circulating Th17 number was shown to be unaffected by healthy pregnancy [23], and increased in pregnancies with adverse outcomes such as preterm labor [24] and recurrent spontaneous abortion [25].

IMMUNOLOGICAL CHANGES IN ASTHMATIC PREGNANCY

Asthma is traditionally considered as an allergic Th2 type inflammation that leads to bronchial hyperresponsiveness, airway obstruction and – in some cases – tissue remodeling [26]. Another cell type involved in the pathogenesis of asthma is the Treg cell which inhibits inflammatory responses induced by CD4+CD25- effector T cells, suppresses Th2 responses to allergen, and prevents airway eosinophilia, mucous hypersecretion, and airway hyperresponsiveness [27]. Atopic asthma is accompanied with reduced circulating Treg

[28,29] and increased circulating Th17 cell prevalence. Zhao et al. showed that abnormal Th17 immunity may be involved in the pathogenesis of allergic asthma. Besides the elevation of Th2 cell prevalence, they demonstrated that the percentages of Th17 cells as well as the concentrations of Th17-related cytokines were higher in peripheral blood of uncontrolled, mostly moderate to severe persistent allergic asthmatics compared to healthy controls [30].

Immunological changes in asthmatic women during pregnancy depend on asthma control. Signs of pregnancy-induced attenuation of allergic responses were found in asthmatic pregnant women with mostly controlled disease. Activated pools within CD4 and CD8 T cells were larger, and the number of natural killer T (NKT) cells was increased both in non-pregnant asthmatic and in healthy pregnant subjects (compared with non-pregnant healthy controls), but in (mostly well controlled) pregnant asthmatics no further lymphocyte activation was observed, suggesting that the immunosuppressive effect of uncomplicated pregnancy may blunt the lymphocyte activation that characterizes asthma [31].

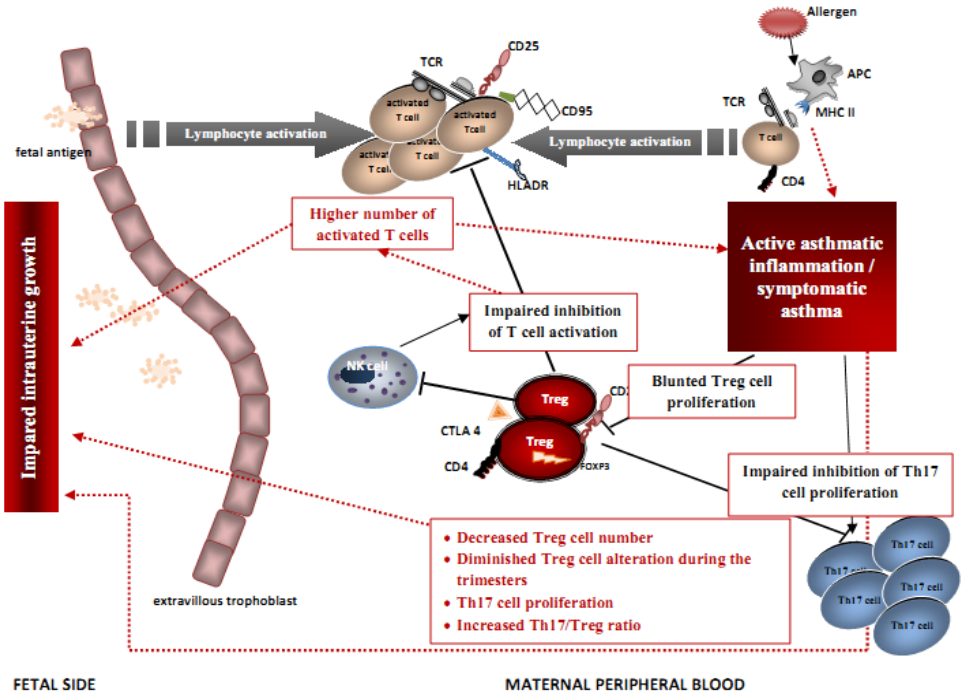

Figure 2. Cellular mechanisms of immune regulation known in asthmatic pregnancy (red arrows) which may lead to compromised physiological fetal growth. Absence of trimester dependent regulatory T (Treg) cell elevation in asthmatic pregnancy results in impaired inhibition of T lymphocyte and NK cell activation and proliferation. Elevated numbers of activated effector T lymphocytes and NK cells may cause immune mediated alteration of fetal growth and enhancement of allergic/asthmatic responses. Asthma-dependent proliferation of circulating T helper 17 (Th17) cells, together with diminished elevation of Treg cells result in an increase in the Th17/Treg ratio characteristic of asthmatic pregnancy (CD - cluster of differentiation; Foxp3 - fork head/winged-helix transcription factor box p3; L – ligand; TCR – T cell receptor; CTLA – cytotoxic T lymphocyte-associated antigen; APC – antigen presenting cell; MHC – major histocompatibility complex antigen HLA – human leukocyte antigen; Treg – regulatory T; Th – T helper; NK – natural killer; → stimulation; ┤ - inhibition).

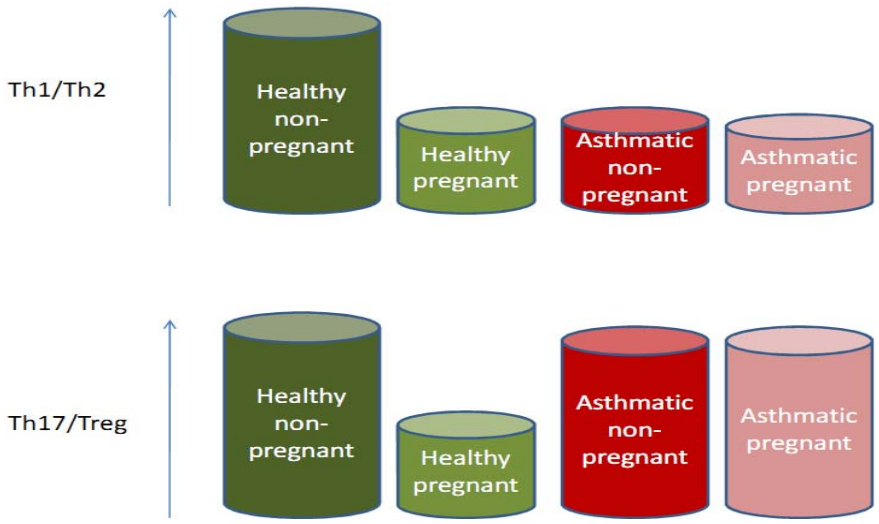

Figure 3. Th1/Th2 and Th17/Treg balance in mostly controlled asthmatic non-pregnant and pregnant patients, compared to healthy non-pregnant and pregnant women (Treg – regulatory T; Th – T helper).

On the other hand, in another study enrolling mostly uncontrolled asthmatic pregnant women, a substantial number of peripheral interferon (IFN)-γ and IL-4 producing cells was detected, and a significant negative correlation was revealed between the numbers of both IFN-γ positive and IL-4 positive T-cells and birth weight of newborns, suggesting that fetal growth restriction (intrauterine growth restriction - IUGR) may be related to active, asthma-associated maternal immune reactions [32]. In addition, considering another inflammatory marker, heat shock protein (Hsp)-70, higher circulating levels were detected in asthmatic than in healthy pregnant women, and fetal birth weight was lower in pregnancies complicated with asthma, again suggesting a relationship between asthmatic immune responses and altered fetal growth [33].

An important determinant of the bidirectional interactions between asthma and pregnancy is the balance of Th1/Th2/Th17/Treg cells. Th1/Th2 cell ratio increases during the pregnancy of not controlled, symptomatic asthmatic women (compared to healthy pregnant women), and remains unaltered in gestations of mostly well or partially controlled patients [23]. Peripheral Treg numbers are elevated in healthy pregnancy, and this elevation is blunted during the gestation of either symptomatic or asymptomatic asthmatic women. Furthermore, the supposed relationship between strengthened maternal immune tolerance and the physiological growth of the fetus is reflected by a positive correlation between maternal Treg numbers and the birth weight of newborns in healthy pregnancy, which is also absent in asthmatic gravid patients [34]. Asthma-dependent elevation of circulating Th17 cell number resulting in a change in the Th17/Treg ratio also plays a role in the altered immunological tolerance characterizing asthmatic pregnancy: the decreased Th17/Treg ratio observed in healthy pregnancy is not observed in asthmatic pregnant women [23]. Immunological changes characterizing asthmatic pregnancy are summarized in Figure 2. Th1/Th2 and Th17/Treg ratios of controlled asthmatic non-pregnant and pregnant patients compared to healthy non-pregnant and pregnant women are shown in Figure 3.

THE EFFECT OF MATERNAL ASTHMA ON PREGNANCY OUTCOMES

Immunological and clinical changes characterizing asthmatic pregnancy affect not only the mother but the newborn as well [35]. In a database cohort of 13100 pregnant asthmatics, a 35% increase in the risk of perinatal mortality was observed in the pregnancies of women with asthma [4]. Major factors contributing to this severe complication seemed to be prematurity and/or low birth weight which were partially caused by uncontrolled asthma, maternal obesity, or smoking [5]. Another recent study of pregnant women with physician-diagnosed asthma evaluated their asthma control repeatedly during pregnancy. According to the results, the incidence of preterm delivery was higher among patients with inadequate asthma symptom control during the first part of pregnancy compared with patients with adequate asthma control. Furthermore patients who were hospitalized for asthma during pregnancy had a higher incidence of preterm delivery compared with asthmatic women without a history of hospitalization. Thus there may be a risk for preterm delivery posed by poorly controlled maternal asthma [8]. According to a population-based cohort of 13007 pregnancies in asthmatic women, mothers with severe and moderate asthma during pregnancy have a higher risk of small for gestational age babies than those with mild asthma [36]. In a recent meta-analysis of 40 publications (involving 1637180 subjects), maternal asthma was associated with an increased risk of low birth weight, small for gestational age, preterm delivery and preeclampsia. The relative risk of preterm delivery and preterm labor were reduced by active asthma management [37].

Data are not consistent regarding the effect of maternal asthma by itself on the development of congenital malformations. However, in a recent large population-based cohort study, maternal asthma was shown to increase the risk of specific groups of congenital malformations such as nervous system (excluding spina bifida), respiratory and digestive system [38]. On the other hand, there are also population-based data that do not show any teratogenic effect of maternal asthma itself [39, 40]. Finally, asthma also affects newborns' morphometry, as asthma severity was associated with an increased head circumference/birth weight ratio in a recent multicenter prospective observational cohort study [41].

In summary, pregnancies in women with asthma need to be considered as high-risk pregnancies, with increased obstetrical surveillance for preeclampsia, preterm labor, intrauterine growth restriction, and fetal mortality. Infants of women with asthma should be followed for an increased risk of neonatal mortality, especially if preterm or of low birth weight. Regarding asthma control, optimal control of asthma during pregnancy may reduce the risk of perinatal complications including perinatal mortality [5].

PREGNANCY INDUCED CHANGES IN ASTHMA CONTROL

Pregnancy may alter the natural course of asthma (Figure 4.). Asthma improves during pregnancy in about one-third, remains the same in another one-third, and worsens in one-third of pregnant women. More severe asthma before pregnancy increases the risk of worsening during pregnancy, and there is a concordance between the courses of asthma during consecutive pregnancies [42]. Asthma-specific quality of life in early pregnancy is related to

subsequent asthma morbidity during pregnancy [43]. Furthermore, asthma exacerbations are more common and more severe in smokers than nonsmokers during pregnancy, suggesting that asthma may pose a greater risk to the fetus in pregnant smokers [44].

Some studies have suggested that the severity of asthma symptoms during pregnancy may also be influenced by fetal gender. Worsened asthma symptoms [45] and higher incidence of IUGR [46] were observed in asthmatic pregnant women with female fetuses. [34]. Obesity is associated with an increased risk of asthma exacerbations during pregnancy as well [3]. Pregnancy induced immunological tolerance may be altered in obese pregnant asthmatic women, as a lower prevalence of naive T cells was observed in obese compared to non-obese asthmatic pregnant patients [34]. In addition, maternal obesity is associated with a higher risk of non-pulmonary complications (e.g. preeclampsia, gestational diabetes, and gestational hypertension) in asthmatic pregnant patients [3].

MANAGEMENT OF ASTHMA DURING PREGNANCY

Diagnosis and Monitoring

The diagnosis of asthma is usually known before pregnancy. However, if symptoms occur for the first time during gestation, reduced forced expiratory volume in one second (FEV1) or ratio of FEV1 to forced vital capacity (FVC) and a 12% or greater improvement in FEV1 after inhalation of rapid acting beta-agonist confirm the diagnosis of asthma. Testing bronchial hyperresponiveness is contraindicated during pregnancy (because of the lack of safety data); thus women with a clinical picture of new-onset asthma without spirometric confirmation of the diagnosis should be treated for asthma during pregnancy. Skin prick tests are not recommended during pregnancy (risk of systemic reactions), but blood tests for specific IgE antibodies to suspected allergens may be evaluated [47].

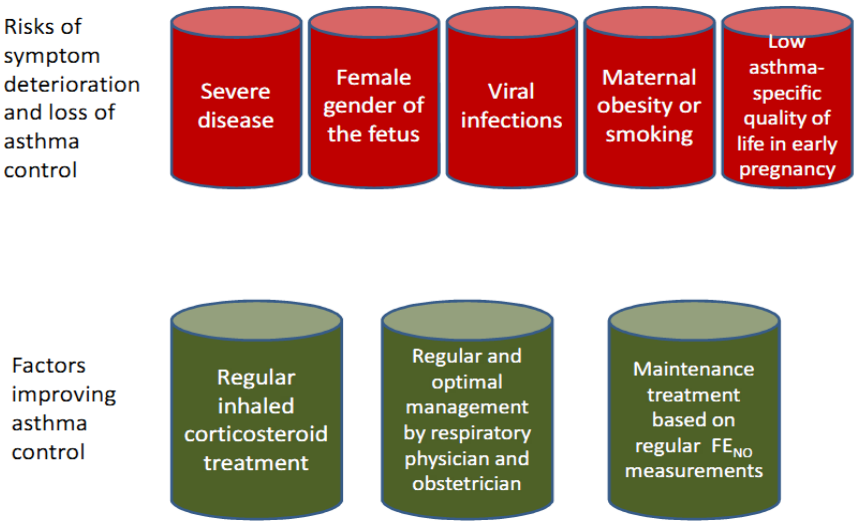

Figure 4. Factors associated with increased risk of asthma deterioration and factors improving asthma control during pregnancy (FE_{NO} - nitric oxide present in exhaled breath).

Due to the bidirectional interactions between asthma and pregnancy and alterations of asthma severity during pregnancy, establishing optimal asthma management during gestation often represents a special challenge for the attending physician. The aim of treatment is to achieve and maintain control of the disease. Fractioned concentration of nitric oxide present in exhaled breath (FE_{NO}) has been evaluated as a non-invasive tool for assessing airway inflammation in asthma [48], and a recent study provided data supporting it's applicability in asthmatic pregnant patients as well [49]. Furthermore it was also recently shown that asthma exacerbations during pregnancy can be significantly reduced with a FE_{NO}-based treatment algorithm in which the doses of inhaled corticosteroids and add-on long-acting beta agonists were based on the results of regular FE_{NO} measurements) [50].

Pregnancy-induced hyperpnea causes somewhat higher arterial oxygen (pO_2 100-105 mmHg) and lower arterial carbon-dioxide (pCO_2 32-34 mmHg) partial pressures during normal pregnancy [51,52]. Thus, even mild maternal hypoxemia may represent respiratory compromise during pregnancy. Generally, maintenance of an arterial oxygen saturation of at least 95% measured by pulse oximetry is recommended to ensure sufficient oxygenation in both the mother and the fetus [47].

Monthly assessments are needed in all asthmatic pregnant women taking regular controller therapy for asthma. The most important assessments that are regularly required in the management of asthmatic pregnant women are the following:

1. asthma control evaluation (Asthma Control Test or similar tool)
2. physical examination
3. spirometry (FE_{NO} evaluation optional, but may help)
4. pulse oxymetry, with access to arterial blood gas analysis if needed, for uncontrolled asthma suggested by any of the above.

Treatment

1. Patient Education

Asthmatic pregnant patients should be educated regarding their disease and its treatment (Table 1.), as recommended in current guidelines [7,47,53]. Active (but not passive) smoking is associated with increased asthma symptoms and fetal growth abnormalities among pregnant women with asthma [52]; thus smoking cessation is necessary for asthmatic pregnant women (not only because of adverse effects of smoking on asthma and on pregnancy but also due to the known higher risk for neonatal asthma in asthmatic pregnant women who smoke [54]).

2. Pharmacological Therapy

Asthma is one of the most frequent causes of drug purchase during pregnancy [55]. Fortunately, most of the data on possible teratogenic effects of asthma medications are reassuring [47]. Although the use of bronchodilators during pregnancy was associated with an increased risk of gastroschisis among infants in one study [39], and higher risk of cardiac defects was observed in newborns of asthmatic mothers in another one [56], it must be noted

that asthma exacerbation itself during pregnancy may increase the risk of congenital malformations [57].

Table 1. Patient educational topics for asthmatic pregnant women*

Main patient educational topics	Description
1. Information about the disease	Basic information about asthma and it's relationship to pregnancy. Facts regarding maternal and fetal outcomes.
2. Use of inhaler devices	Demonstration of correct use of devices prescribed to the patient.
3. Adherence to treatment and importance of regular visits	Necessity of regular visits and appropriate controller medication during pregnancy complicated with asthma.
4. Environmental control measures to reduce exposure to allergens and irritants	Avoidance of known allergens and smoking.
5. Self-treatment action plan	Written schedule for maintenance therapy and doses of rescue medication for increased symptoms. Education about signs of asthma exacerbation and seeking urgent or emergency care. Education about controller medication increase or oral corticosteroid use for increased symptoms.

* reprinted with permission from reference 47.

A matched case-control analysis showed no increased risk of malformation with gestational exposures to short- or long-acting beta agonists, inhaled corticosteroids, oral corticosteroids, other bronchodilators or cromones. These findings were similar for each of the system-specific malformation groups, except for an increase in musculoskeletal system malformation associated with cromone exposure [40]. Summing up, observational studies of using inhaled beta-agonists and inhaled corticosteroids during pregnancy showed no increase in perinatal risks or congenital malformations [58,59,60,61].

Taking into consideration all risks (congenital malformations and adverse perinatal outcomes), according to currently available safety data, albuterol is the reliever medication of choice during pregnancy. The first choice controller anti-asthmatic treatment during pregnancy is inhaled corticosteroid (ICS) therapy. A recent cohort formed of 4140 women who used 0 to 250 μg/day ICS and 1140 women who used greater than 250 μg/day ICS (together with 7724 nonusers of ICS) during pregnancy showed no association between ICS use (any dose) during pregnancy and perinatal mortality [62]. Budesonide is the preferred inhaled corticosteroid based on available data in human pregnancies [63, 64]. However no increase in adverse pregnancy outcomes has been reported in subjects using beclomethasone or fluticasone compared with non-asthmatic controls [65]. Basically, any ICS that results in optimal control of the disease before pregnancy should be maintained during gestation [65]. Long-acting inhaled beta-agonists (formoterol and salmeterol) may be used as add-on therapy in pregnant patients if symptoms occur despite regularly used inhaled corticosteroid therapy. Leukotriene-receptor antagonists (montelukast and zafirlukast) also seem to be safe during gestation, but the available human data are limited [9]. In one recent study enrolling 180

asthmatic pregnant women taking montelukast, no increase in the rate of major congenital malformations was observed [66]. On the other hand, the oral corticosteroids may adversely affect pregnancy outcomes. One study found that 2.4% of pregnant asthmatic women used oral corticosteroids at some time of pregnancy [67]. There are data supporting the association of systemic corticosteroid exposure with preeclampsia, preterm birth, and reduced birth weight of newborn [68]. Although case-control studies have found an association between maternal first trimester systemic corticosteroid exposure and oral clefts [69], a recent large cohort study did not confirm this association [70].

Treatment of asthma during pregnancy must be aimed at controlling the disease (symptoms and lung function abnormalities as well) [69]. Asthmatic women with well-controlled asthma should continue taking their medications during pregnancy. Although guidelines recommend consideration of a step down in therapy in non-pregnant patients with well-controlled asthma for at least 3 months [7,9], controller treatment may be maintained in pregnant patients in order to reduce the risk of loss of asthma control during pregnancy. Therapy should be increased by one step in patients with asthma that is not well controlled (Table 2). A two-step increase, a course of oral corticosteroids, or both should be recommended for women with asthma that is very poorly controlled (Table 2.) [47].

Table 2. Steps of asthma maintenance therapy during pregnancy* (LTRA – leukotriene-receptor antagonist; LABA – long-acting beta-agonist)

Step	Preferred controller medication	Alternative controller medication
1	None	-
2	Low-dose inhaled corticosteroid	LTRA, cromones, theophylline
3	Medium-dose inhaled corticosteroid	Low-dose inhaled corticosteroid + LABA or LTRA or theophylline
4	Medium-dose inhaled corticosteroid + LABA	Medium -dose inhaled corticosteroid + LTRA or theophylline
5	High-dose inhaled corticosteroid + LABA	-
6	High-dose inhaled corticosteroid + LABA + oral corticosteroid	-

* reprinted with permission from reference 47.

Monthly asthma control assessment is recommended for women who require controller therapy during pregnancy. Optimal obstetrical care of not well controlled asthmatic pregnant patients means more frequent ultrasonographic examinations (to monitor fetal growth, which can be affected by uncontrolled asthma) and assessments of fetal well-being (nonstress testing from the 32nd gestational week). During labor and delivery the use of asthma medications should be continued. Women who are currently taking systemic corticosteroids or who have received several short courses of systemic corticosteroids during pregnancy are recommended to get intravenous corticosteroids during labor and for 24 hours after delivery [47].

3. Acute Asthma Exacerbations

Asthma exacerbations during pregnancy represent a major challenge to the attending physicians. They occur in about 20% of asthmatic pregnant women, with approximately 6%

of women being admitted to hospital [70]. Exacerbations during pregnancy occur primarily in the late second trimester; the major triggers are viral infection and non-adherence to inhaled corticosteroid medication [70]. Women who have a severe exacerbation during pregnancy are at a significantly increased risk of having a low birth weight baby compared with women without asthma. Furthermore, acute exacerbations during pregnancy increase the risk of perinatal mortality as well [70]. Exacerbations in the first trimester of pregnancy increase the risk of congenital malformations [57]. For the above reasons, preventing acute asthma exacerbations with optimal controller anti-asthmatic therapy (regular inhaled corticosteroid treatment in most cases) is an extremely important goal of asthma treatment during pregnancy.

Effective, rigorous treatment of an asthma exacerbation occurring in an asthmatic pregnant woman is important for the health of both the mother and fetus; however in everyday clinical practice pregnant asthmatics are less likely to receive appropriate treatment with corticosteroids [71]. Cooperation between the respiratory specialist and obstetrician is essential. The patient should receive close monitoring of lung function, oxygen saturation should be maintained above 95%, and fetal monitoring should be considered. The principles for the therapy of acute asthma during pregnancy are similar to those for management in the non-pregnant state. Repeated doses of inhaled/nebulized beta2-agonists and ipratropium bromide, and the early administration of systemic corticosteroids (intravenous methylprednisolone), together with oxygen supplementation and intravenous magnesium if needed are the cornerstones of therapy [51]. Status asthmaticus requiring mechanical ventilation is an uncommon, life-threatening disorder in obstetric patients; however, there are reports of excellent pregnancy outcomes after mechanical ventilation started due to severe respiratory acidosis in acute asthma exacerbation during pregnancy [72].

CONCLUSION AND SUMMARY

Asthma is one of the most common chronic diseases complicating pregnancy and influencing its outcome. Attenuation of allergic responses can be detected in controlled asthmatic pregnant patients supporting the presence of pregnancy-induced immune tolerance. However, uncontrolled asthmatic pregnant women show significant asthma-associated immune reactions, such as diminished pregnancy specific regulatory T cell proliferation and elevation of Thelper-17 cell numbers. Generally, although uncontrolled asthma may increase the risk of adverse perinatal outcomes (including higher risk of perinatal mortality, pre-eclampsia, preterm birth and impaired fetal growth), women with adequately-treated and well-controlled disease during pregnancy do not appear to be at increased risk of maternal or fetal complications. Controlling asthma during pregnancy with appropriate medications leads to improved intrauterine growth of the fetus and fewer adverse outcomes. Medications used to treat asthma, such as bronchodilators (short-acting β2-agonists) and controller medications (especially inhaled corticosteroids), have no effects on fetal growth. Although taking oral corticosteroids during pregnancy may confer an increased risk of lower birth weight and congenital malformations, benefit risk considerations still favor their use in patients with uncontrolled severe chronic asthma or asthma exacerbations. Frequent communication between obstetricians, asthma specialists, and general practitioners is vital in the treatment of

asthma during pregnancy, as well as the development of an effective partnership between the patient and her health care professionals.

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