

The Effect of Pregnancy on the Course of Asthma

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Bronchial asthma is a chronic disease whose incidence and mortality increased by more than 30% in the 1980s, with a threefold increase in women aged 18 to 24 years in the 1990s [1,2]. The course of bronchial asthma is one of exacerbation and remission that is caused by a cascade of events. Airway inflammation (with infiltration of inflammatory cells, such as eosinophils, lymphocytes and mast cells) leads to increased airway responsiveness and airway obstruction. Multiple intrinsic and extrinsic factors can influence the course of asthma, all of which can occur concomitantly with pregnancy.

Asthma is the most common chronic pulmonary disease, and complicates approximately 4% to 8% of all pregnancies [2]. This percentage varies depending on the specific questions that are used in surveys. The effect of pregnancy itself on asthma has been evaluated in many studies over the years. The general conclusion by Juniper and Newhouse [3], who used meta-analysis to evaluate retrospective and prospective studies, is that one third of women have improvement of asthma during pregnancy, one third experience no change, and one third have a worsening of their asthma. Severe asthmatics, even those under good medical control before pregnancy, are more likely to experience severe exacerbations during pregnancy [4].

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Normal physiologic changes of pregnancy and their effects on asthma

There are many physiologic changes that occur during pregnancy. Some of these could have beneficial effects on the course of asthma and others could be deleterious (Box 1) [5]. The exact effects of these physiologic changes on the course of asthma during pregnancy are unknown.

Respiratory tract

The impact on the respiratory tract is physical and functional during pregnancy. The diaphragm rises about 4 cm, the transverse diameter of the thoracic cage increases about 2 cm, and the thoracic circumference increases about 6 cm. There is a significant reduction in expiratory reserve volume and residual volume of air in the lungs, especially in the last trimester. By term, there is a 17% to 25% decrease in functional residual capacity [6].

Tidal volume, minute ventilatory volume, and minute oxygen uptake increase substantially by the last trimester, although respiratory rate changes little (Table 1) [7,8]. The most consistent respiratory change is an increase of almost 50% in minute ventilation, which is caused by stimulation of the respiratory center by increasing concentrations of progesterone [9]. Oxygen consumption increases 21% to 35% and peaks late in pregnancy [10].

Dyspnea occurs in 60% to 70% of pregnant women in the first and second trimesters. This dyspnea is believed to be due to the increase in tidal volume that lowers blood PCO_2 and causes increased respiratory effort that is induced by progesterone and estrogen. Pulmonary function is not impaired in normal pregnant women, but the sensation of dyspnea may cause apprehension and exacerbation in pregnant asthmatics. The decreased pulmonary reserve and increased respiratory effort also may cause increased asthma [7].

The upper respiratory tract also is affected in pregnancy. Marked congestion of the inferior nasal turbinates (stuffy nose of pregnancy) that lasts for at least 10 days and is not caused by viral infection or allergy was reported to occur in 22% to 72% of all pregnancies [11,12]. Symptoms begin most often during 20 to 22 weeks of gestation. Nearly all women improve by 2 to 4 weeks post partum.

A prospective study of 568 pregnant asthmatics showed a significant correlation between the course of gestational asthma and the course of rhinitis during pregnancy. In those patients who had less asthma during pregnancy, 51% had fewer rhinitis symptoms, whereas 20% had increased rhinitis. Only 2% of patients whose asthma worsened reported less rhinitis, and 56% had increased rhinitis. In patients whose asthma did not change during pregnancy, 27.5% had increased rhinitis [13].

Gastroesophageal reflux

In asthma, reflux is associated with disease exacerbation, and medical and surgical treatment of reflux has resulted in a decrease in asthma symptoms [14].

Box 1. Physiologic changes during pregnancy that may affect the course of asthma*Factors that may improve asthma*

Progesterone-mediated bronchodilation
Decreased plasma-histamine-mediated bronchoconstriction
(due to increased circulating histaminase)
Estrogen- or progesterone-mediated potentiation of β -adrenergic
bronchodilation
Pulmonary effects of increased serum-free cortisol
Glucocorticosteroid-mediated increased β -adrenergic
responsiveness
Prostaglandin I_2 -mediated bronchial stabilization
Atrial natriuretic factor-induced bronchodilatation
Increased half-life or decreased protein binding of endogenous
or exogenous bronchodilators
Prostaglandin E-mediated bronchodilation (in the last 4 weeks)
Descent of fetus (in the last 4 weeks)

Factors that may worsen asthma

Pulmonary refractoriness to cortisol effects because of competitive binding to glucocorticosteroid receptors by progesterone, aldosterone, or deoxycorticosterone
Prostaglandin $F_{2\alpha}$ -mediated bronchoconstriction
Decreased functional residual capacity with resultant airway closure during tidal breathing and altered ventilation-perfusion ratios
Increased pulmonary capillary permeability
Increased upper airway resistance from nasal turbinate congestion
Increased placental major basic protein reaching the lung
Increased viral or bacterial respiratory infections triggering asthma exacerbations
Increased gastroesophageal reflux-induced asthma
Increased stress
Elevation of the diaphragm from the expanding uterus (in second and third trimesters)

Modified from Schatz M. Asthma during pregnancy: interrelationships and management. *Ann Allergy* 1992;68:123–33.

Table 1
Pulmonary function in pregnancy and postpartum

Function	10 week	24 week	36 week	Postpartum
Respiratory rate (breaths/min)	15–16	16	16–17	16–17
Tidal volume (mL)	600–650	650	700	550 ^a
Residual volume (L)	1.2	1.1	1.0	1.2 ^a
Vital capacity (L)	3.8	3.9	4.1	3.8

^a Significant difference compared with pregnant state.
Data from Spatling L, Fallenstein F, Huch A, et al. The variability of cardiopulmonary adaptation to pregnancy at rest and during exercise. *Br J Obstet Gynaecol* 1992;18:99(Suppl 8):99.

The increase in serum progesterone during pregnancy causes relaxation of the smooth muscle in the lower esophageal sphincter, which results in reflux, heart-burn, and indigestion in one third of all pregnancies [15,16]. This reflux could exacerbate gestational asthma and may require treatment during pregnancy.

Hormonal changes

There are significant changes in estrogen and progesterone levels during pregnancy. Progesterone levels increase at least 10-fold between the sixth and thirty-sixth weeks of pregnancy. Estrogen levels also increase, with 100 times more estradiol and 1000 times more estriol at term compared to nonpregnant state. Progesterone levels decrease sharply immediately before delivery, and increase uterine contractility.

Elevated progesterone reduces the contractility of smooth muscle in the uterus [17]. It has not been shown that it has a similar effect on pulmonary smooth muscle, but in the last 4 weeks of pregnancy, asthmatics have reduced wheezing, sleep interference, and interference with activities [18].

Fetal effects

The fetus is antigenically foreign to the mother. An exchange of cells between mother and fetus occurs in 10% to 20% of normal pregnancies. In view of this exchange, an inappropriate response to fetal antigens could provoke increased asthma [19]. In addition, emboli of placental trophoblasts are shed into the maternal circulation from early pregnancy. These trophoblasts lodge in capillary beds of the mother's lungs, but the local response is unknown [20].

In an attempt to explain the variations in asthma course during pregnancy, 34 women who delivered a boy and a girl were studied by retrospective questionnaires [21]. The sex of the fetus did not affect the course of asthma in this study. In contrast, in a prospective study, the women with female fetuses had more asthma symptoms. Male fetuses produce a surge of androgens at weeks 12 to 16; this may be a factor in this interesting observation [21].

Course of asthma during pregnancy

Retrospective studies

It is important to recall that for many years, obstetricians and their patients stopped all treatment as soon as pregnancy began. Asthma was not regarded as a high-risk condition, so it is likely that more women had severe difficulty with their asthma because of lack of treatment. In the 1966 edition of *Williams Obstetrics*, the entire subject of asthma and pregnancy is discussed in just two paragraphs [22]. Relying on one retrospective study [23], it stated that pregnancy had no effect on asthma in most cases. No mention is made of any specific problems with asthma during pregnancy or any specific treatment.

The changes in asthma symptoms during pregnancy were reported in several retrospective (mostly case) studies from 1930 to 1967 [23–30]. In these studies of 25 or more women, comprising 1087 pregnancies, 36% had improved symptoms, 41% had unchanged symptoms, and 23% had worsened symptoms during pregnancy [6].

There was a marked difference in results from different investigators (Table 2). There was a beneficial effect of pregnancy on asthma in from 3% to 50% of patients. There was no effect in from 15% to 93% of patients, and an adverse effect was reported in from 4% to 54% of patients. These subjects were found by chart review [26,28,30,31] or by interview up to several years after their pregnancy [23–25]. The changes in the course of asthma were determined by reviewing medication requirements, symptoms, and hospitalizations.

Patients who were studied by Jensen [24], Gandevia [25], Gammal and Warraki [28], Hiddlestone [31], and Williams [30] came from asthma or allergy clinics. These clinics may have been biased toward women who had more problematic asthma and included fewer mild asthmatics. For example, Jensen [24] excluded 22 of (a potential) 106 women because their allergic disease was quiescent during pregnancy. Because these patients came from asthma clinics,

Table 2
Effect of pregnancy on asthma: retrospective studies

First author (country) [ref]	Improved (%)	Same (%)	Worse (%)
Jensen (Denmark) [24]	41	15	44
Gandevia (Australia) [25]	48	28	24
Turiaf (France) [26]	50	26	24
Schaefer (USA) [23]	3	93	4
Gammal (Egypt) [28]	35	25	40
Hiddlestone (N Zealand) [31]	39	35	27
Williams (UK) [30]	42	34	24
Williamson (USA) [27]	20	36	54
Fein (USA) [29]	10	67	23
AVERAGE	36	41	23

Data from Gluck JC, Gluck PA. The effects of pregnancy on asthma: a prospective study. *Ann Allergy* 1976;37:165.

their diagnosis probably was correct. The course of asthma during pregnancy was assessed through changes in their medications. Asthma was said to be worse if medication use increased, and was considered improved if medication use decreased. Over time, asthma treatment has changed. In the past, medications would not have included inhaled steroids, which are a mainstay of treatment today. Thus, evaluation of older studies may not be comparable to evaluation of more recent series.

Other retrospective studies included patients from obstetric clinics [23] or general clinics [26]. These women generally were not comanaged with an asthma specialist. Some of these patients could have been misdiagnosed. In addition, the use of appropriate asthma medication was less likely.

The severity of asthma before or after pregnancy was not noted in any of these studies. Pulmonary function testing as an objective measure was not always available, so the physician's and patient's clinical assessments were relied on to evaluate changes in the course of asthma. The course of asthma during pregnancy as determined from these early studies definitely is variable. Local environmental conditions probably are not a factor because there were similar data from different locations.

Prospective studies

Since 1976, several studies have evaluated the course of asthma during pregnancy prospectively. The latest edition of *Williams Obstetrics* advised that the "treatment of acute asthma during pregnancy is similar to that for the nonpregnant asthmatic" [47]. In pregnant patients, undertreatment of asthma, owing to fears of adverse effects on the fetus, continued to be a major problem, especially among obstetricians. Most patients in these prospective studies were enrolled from maternity clinics and were followed through delivery and into post partum [4,6,18,32,33]. One study enrolled patients from an asthma clinic before pregnancy and used nonpregnant female controls [34]. The criterion for entry into the studies was a history of asthma. Three studies included a control cohort of pregnant, nonasthmatic women, which is more helpful in assessing the effect of asthma on pregnancy. Patients reported their prepregnant condition, and many were followed post partum, which served as another control. Again, when the

Table 3
Effect of pregnancy on asthma: prospective studies

Study	<i>n</i>	Improved (%)	Same (%)	Worse (%)
Gluck [6]	47	14	43	43
Schatz [18]	330	28	33	35
Stenius-Aarniala [32]	198	18	40	42
White [33]	31	69	22	9
Juniper [34]	16	50	37.5	12.5
Schatz [4]	1624	23	47	30
AVERAGE	2246	33.6	37	28.5

total population of asthmatics in these studies is considered, about one third were improved, one third were unchanged, and one third were worse (Table 3).

Six prospective studies followed the course of asthma through pregnancy. Of those, five stratified their subjects according to the severity of asthma at the beginning of pregnancy [4,6,32–34]. Gluck and Gluck [6] followed all patients who had a history of asthma from their first visit to a prenatal clinic. Patients were stratified by severity of asthma based on frequency of symptoms before pregnancy. Severe asthmatics (12 patients) had symptoms at least weekly. Moderate asthmatics (10 patients) had attacks at least monthly, but not as frequently as the severe group. Those who had symptoms less often than monthly, but with a history of one or more attacks within the preceding 5 years, were considered mild asthmatics (25 patients).

In contrast, Stenius-Aarniala and colleagues [32] divided their patients by severity based on medication requirements and clinical course during pregnancy (Table 4). White and colleagues [33] stratified a group of 31 patients at the time of entry based on medication usage. Mild asthmatics required only occasional bronchodilators, moderate asthmatics used bronchodilators more than half of the days or required inhaled steroids, and severe asthmatics required oral steroids. Only one was considered to have severe disease, and more than half (17/31) had mild disease.

Juniper and colleagues [34] divided their patients based on medications that were required to control asthma symptoms. They used statistical analysis that was based on the class of drug and dosage, and methacholine challenge. There were 5 mild asthmatic patients, 1 moderate asthmatic patient, and 10 severe asthmatic patients in this study. The clinical course of asthma during pregnancy was assessed for the group overall. Eight patients improved, 6 were unchanged, and 2 deteriorated. In addition, using the methacholine challenge, they documented objective changes during pregnancy.

Schatz and colleagues [4] evaluated pregnant patients at less than 25 weeks' gestation who reported asthma symptoms in the previous 6 months. Frequency of asthma symptoms in the past month, forced expiratory volume in 1 second (FEV₁), and daily medications were assessed on entry into the study. The patients were divided into mild (873), moderate (814), and severe (52) categories. When

Table 4
Classification of asthma severity during pregnancy

Group (n)	Medication	Exacerbation	Hospitalization
Very mild (56)	None or inhaled bronchodilators, sodium cromoglycate or beclomethasone	None	None
Mild (52)	As above plus oral bronchodilator	None	None
Moderately severe (56)	As above	One or more	None
Severe (34)	As above	One or more	One or more

Data from Stenius-Aarniala B, Piirila P, Teramok K. Asthma and pregnancy: a prospective study of 198 pregnancies. Thorax 1988;43:13.

assessing the change in asthma during pregnancy overall, 23% improved, 47% were unchanged, and 30% were worse.

Because the course of asthma during pregnancy is related to the severity of asthma (see later discussion), variations in findings among studies can be attributed, at least in part, to the different proportions of the asthma severity subgroups. In the two studies that had a similar severity distribution [6,32], the results regarding asthma course were similar.

Severity

When the course of asthma was evaluated in patients who had mild asthma with occasional wheezing and bronchodilator usage, most showed no change in their disease. Gluck and Gluck [6] found that 72% of mild asthmatics were unchanged during pregnancy, 16% worsened, and 12% improved. Stenius-Aarniala and colleagues [32] found that 22% of mild asthmatics were worse during pregnancy and improved after delivery. Schatz and colleagues [4] classified patients as having mild asthma if they had fewer than 8 days of symptoms in the 4 weeks before enrollment, no daily medications, and an FEV₁ of 80% or greater. Of these 873 patients, 28% were worse during their pregnancy, whereas the others' disease remained mild. The patients in White and colleagues' study [33] were mild or moderately severe at the start of pregnancy; most of these patients improved or had no change in severity. Improvement was noted especially in the third trimester in peak flow measurements and the perception of asthma symptoms. Thus, it seems that patients who have mild asthma before pregnancy usually do not experience exacerbation of the disease during pregnancy.

When severe asthmatics were evaluated, a different picture emerged. Gluck and Gluck [6] found that none of their severe asthmatics improved during pregnancy, 17% were unchanged, and 83% were worse, with nine hospitalizations for status asthmaticus in 12 patients. In the larger study by Stenius-Aarniala

Table 5
Asthma morbidity during pregnancy after enrollment in the study in relationship to initial asthma severity classification

Asthma severity	Hospitalized for asthma	Unscheduled visit ^a	Oral corticosteroid for asthma	Exacerbation ^b	Asthma symptoms during labor/delivery
Mild (n=873)	20 (2.3%)	99 (11.3%)	19 (2.2%)	110 (12.6%)	116 (13.3%)
Moderate (n=814)	55 (6.8%), <i>P</i> <.0001 ^c	157 (19.3%), <i>P</i> <.0001	71 (8.7%), <i>P</i> <.0001	209 (25.7%), <i>P</i> <.0001	171 (21.0%), <i>P</i> <.0001
Severe (n=52)	14 (26.9%), <i>P</i> <.0001	19 (36.5%), <i>P</i> =.003	20 (38.5%), <i>P</i> <.0001	27 (51.9%), <i>P</i> <.0001	24 (46.2%), <i>P</i> <.0001

^a Includes unscheduled antenatal, primary care or emergency department visit for asthma.
^b Hospitalization, unscheduled visit, or oral corticosteroid course for asthma.
^c *P* values indicate comparison to group directly above.

From Schatz M, Dombrowski MP, Wise R, et al. Asthma morbidity during pregnancy can be predicted by severity classification. *J Allergy Clin Immunol* 2003;112:285; with permission.

and colleagues [32], the most severe asthmatics had significantly lower FEV₁ and maximum flow at 50% vital capacity measurements during the last month of pregnancy. When surveyed post partum, 34.5% of all patients believed that their asthma was better than during pregnancy. Most of the patients who had severe asthma (56%) felt better after delivery. A large multicenter study of women who had moderate asthma (defined as 8 or more days of symptoms in the previous 4 weeks, daily medication [not oral steroids], and an FEV₁ of 60%–80% of predicted) found that they had more symptoms than did mild asthmatics, and less symptoms than did severe asthmatics during pregnancy (Table 5) [4]. Patients who had severe asthma, defined as an FEV₁ of less than 60% of predicted or who took daily oral steroids, had the most asthma morbidity of all patients studied (Table 6). Grouping moderate and severe asthmatics together, 77% were unchanged and 23% had milder symptoms in pregnancy [4]. These studies show that the course of asthma in pregnancy varies with the severity of asthma before pregnancy, regardless of previous treatment. Women who have more severe asthma tend to have exacerbations of their disease with more symptoms and medications required than in women who have milder disease.

Stage of pregnancy

All stages of pregnancy are not the same for patients who have asthma. The first trimester generally is tolerated well in asthmatics who have only rare exacerbations [6,18,33,34]. Gluck and Gluck [6] found that increased symptoms did not occur before the fourth month of gestation, and the peak incidence of flares occurred during the sixth month, regardless of the severity of the asthma.

Table 6

Asthma morbidity for the entire pregnancy in relationship to the change in initial versus final asthma severity classification

Initial/final asthma severity	Hospitalized for asthma	Unscheduled visit ^a	Oral steroid for asthma	Asthma exacerbation ^b	Asthma symptoms during labor/delivery
Mild/mild (n = 565)	11 (2.0%)	75 (13.3%)	3 (0.5%)	80 (14.2%)	60 (10.6%)
Mild moderate or severe (n = 246)	21 (8.5%), <i>P</i> < .0001 ^c	83 (33.7%), <i>P</i> < .0001	20 (8.1%), <i>P</i> < .0001	92 (37.4%), <i>P</i> < .0001	45 (18.3%), <i>P</i> = .0028
Moderate or severe/moderate or severe (n = 627)	107 (17.1%)	264 (42.1%)	110 (17.5%)	310 (49.4%)	155 (24.7%)
Moderate or severe/mild (n = 186)	9 (4.8%), <i>P</i> < .0001	50 (26.9%), <i>P</i> = .0002	3 (1.6%), <i>P</i> < .0001	57 (30.7%), <i>P</i> < .0001	31 (16.8%), <i>P</i> = .0216

Includes only patients with more than 30 days of follow-up data.

^a Includes unscheduled antenatal, primary care, or emergency department visit for asthma symptoms.

^b Hospitalization, unscheduled visit, or oral corticosteroid course for asthma.

^c *P* values indicate comparison to group directly above.

From Schatz M, Dombrowski MP, Wise R, et al. Asthma morbidity during pregnancy can be predicted by severity classification. *J Allergy Clin Immunol* 2003;112:286; with permission.

Schatz and colleagues [18] found an increase in symptoms between 29 and 36 weeks' gestation in women whose asthma was worse during pregnancy. Juniper and colleagues [34] also found an increase in symptoms in the second and third trimesters compared with preconception in 5 of 16 patients. Using methacholine challenge, objective changes were documented during pregnancy that showed improvement in the second trimester in the group as a whole [34]. Stenius-Aarniala and colleagues [35] found that most acute exacerbation occurred between 17 and 24 weeks of pregnancy.

In the last month of pregnancy, asthma improves in many mild-moderate asthmatics [18,33]. Stenius-Aarniala and colleagues [32] found lower FEV₁ measurements in the last month of pregnancy in patients who had severe asthma, but patients were less likely to have exacerbations at this time. Schatz and colleagues [18] assessed asthma symptoms at 4-week intervals throughout pregnancy; fewer and less severe symptoms were found in the last 4 weeks of pregnancy than during any other interval (Fig. 1). Even among women whose asthma worsened during pregnancy, there was relative improvement in the last 4 weeks (Fig. 2) [18]. These studies suggest that the first trimester and the last month of pregnancy are mostly free of asthma exacerbations, and that the second and earlier part of the third trimesters have more potential for increased asthma symptoms.

In labor and delivery

Approximately 10% to 20% of asthmatics have asthma symptoms during labor and delivery [4,18]. These symptoms usually are mild and can be controlled

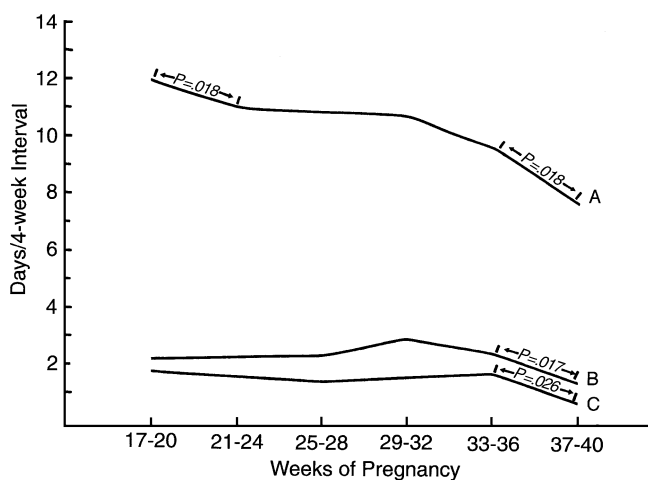


Fig. 1. Mean number of symptomatic days (total days of wheezing [A], days of sleep interference [B], days of interference with normal activity [C]) versus 4-week gestational intervals in 75 women (P values for significant differences noted). (From Schatz M, Harden K, Forsythe A, et al. The course of asthma during pregnancy, post partum, and with successive pregnancies: a prospective analysis. *J Allergy Clin Immunol* 1988;81:511; with permission.)

easily [32]. In one study of 360 patients, 37 patients were symptomatic during labor and delivery. Of these, 54% required no treatment, 41% used inhaled bronchodilators, and 5% were given intravenous aminophylline [18]. The incidence of asthma symptoms during labor and delivery increases with increased asthma severity, and there are significant differences between patients who have mild (12.3%), moderate (22.4%) and severe (44.4%) disease [4]. Mabie and

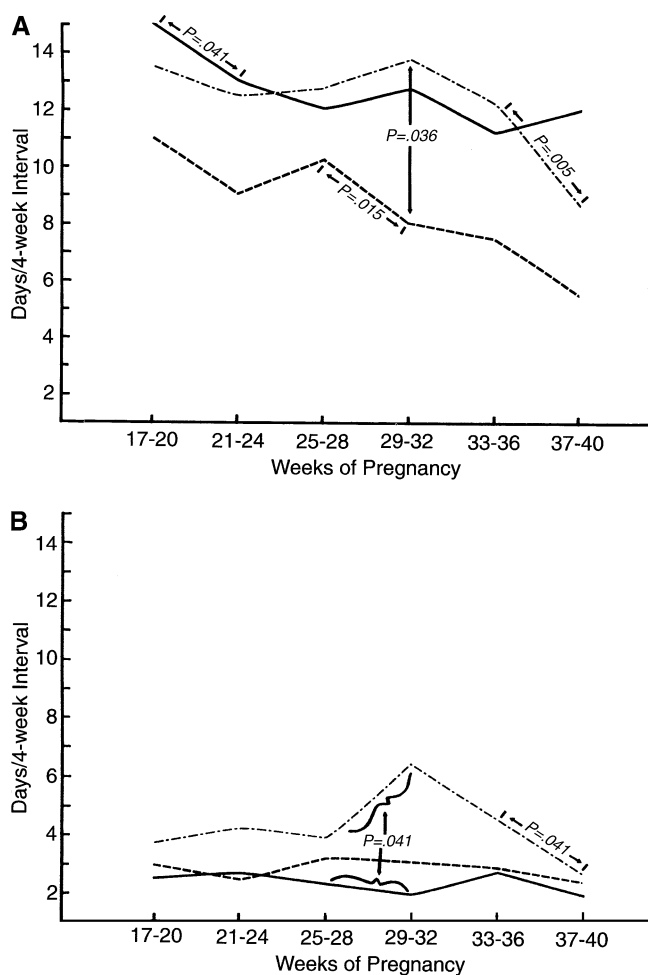


Fig. 2. Mean number of symptomatic days versus 4-week gestational intervals in each of 25 women whose asthma got worse (*dot-dash line*), got better (*dashed line*), or stayed the same (*solid line*) during pregnancy (P values for significant differences are noted) (A) Total days of wheezing. (B) Days of interference with sleep caused by asthma. (C) Days of interference with normal activity caused by asthma. (From 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;81:512; with permission.)

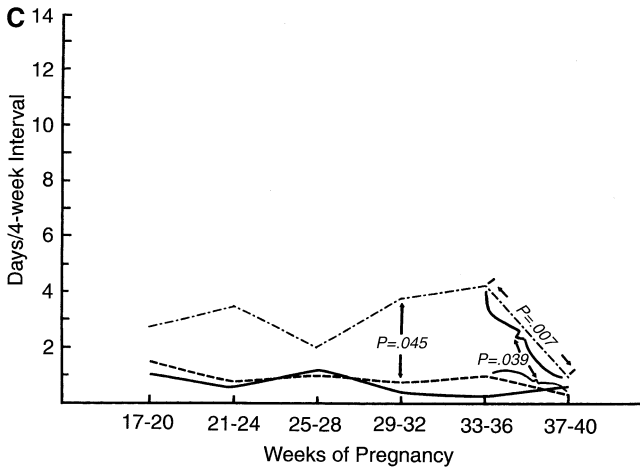


Fig. 2 (continued).

colleagues [36] reported an 18-fold increased risk for asthma exacerbation during delivery by cesarean section compared with vaginal delivery.

Course of asthma post partum

In general, after delivery, asthma returns to the severity that was present before pregnancy. If the course of asthma during pregnancy was unchanged, the disease remained the same after delivery in 72% of the women studied. When asthma changed during pregnancy, it returned to the prepregnancy state within 3 months in 74% of women (Fig. 3) [18]. Similarly, 56% of women who had severe asthma during pregnancy had fewer symptoms after delivery, whereas only 22% of mild asthmatics improved after giving birth [32]. These data support the concept that the changes in the course of asthma during pregnancy are more than just random fluctuations in its natural course. Several other studies observed that asthma changes that occurred during pregnancy disappeared within 3 months after delivery [6,24,25,33,34].

Course of asthma during subsequent pregnancies

Several studies found that the course of asthma in individual women is similar during subsequent pregnancies. Gammal and Warraki [28] reported consistency in deterioration in 29 of 33 patients and consistent improvement in 23 of

28 patients. Williams [30] found that 63% of his patients had similar courses; all of Jensen's [24] patients had consistent courses of asthma during subsequent pregnancies. Stenius-Aarniala and colleagues [32] followed 13 women through two pregnancies, but adjusted medications at an earlier stage in the second pregnancy, which led to better asthma control. Schatz and colleagues [18] noted

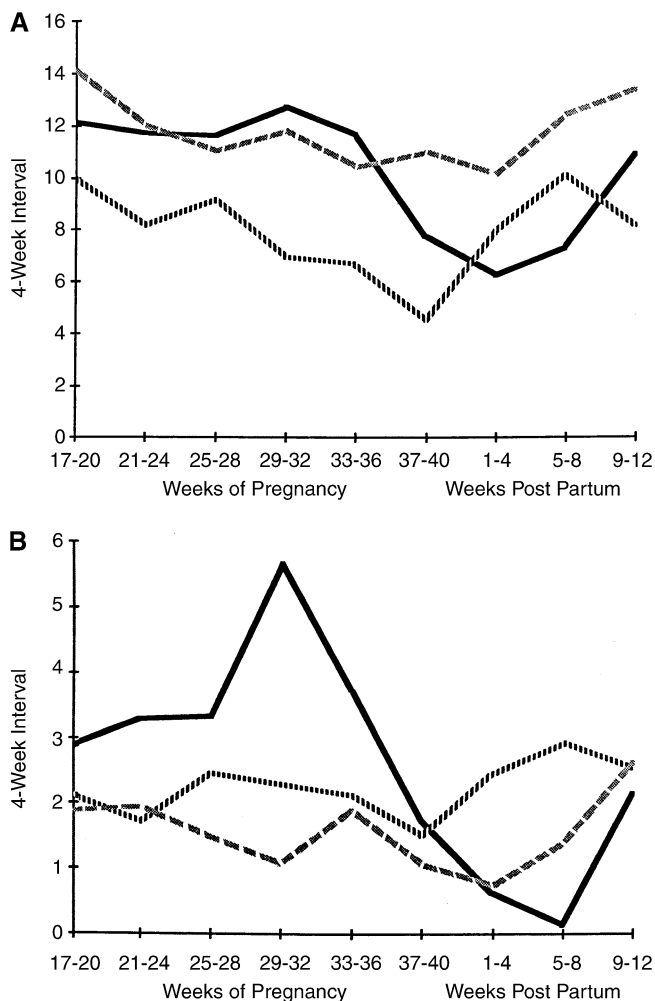


Fig. 3. Mean number of symptomatic days versus 4-week intervals from 17 weeks of pregnancy to 12 weeks post partum in each of 25 women whose asthma got worse (*solid line*), got better (*hatched line*) or stayed the same (*dashed line*) during pregnancy. (A) Total days of wheezing. (B) Days of sleep interference caused by asthma. (C) Days of interference with normal activity caused by asthma. (From 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; 81:513; with permission.)

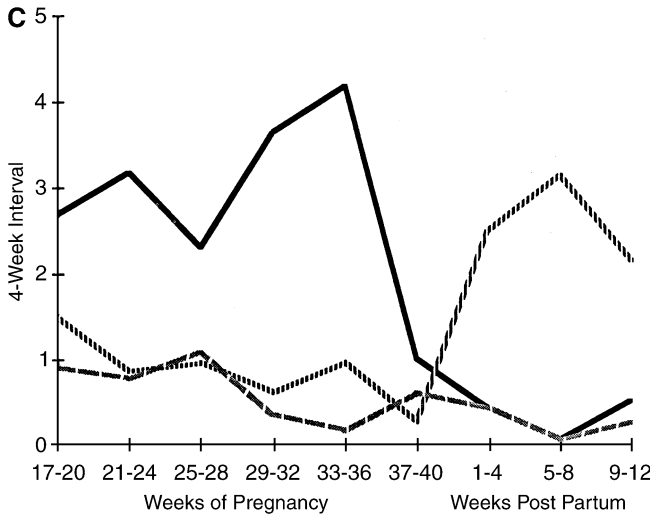


Fig. 3 (continued).

exact concordance in the course of asthma in 58.8% of 34 women who were seen through two pregnancies.

Other factors that affect asthma during pregnancy

Reluctance to treat

Asthma severity and control of asthma are important risk factors during pregnancy. Factors, such as reluctance to treat, result in poor control of asthma during pregnancy. Additionally, decreased compliance may occur because of a patient's concerns about the safety of medication for the fetus.

A study of treatment of acute asthma in emergency departments across the United States included 551 women (51 pregnant and 500 not pregnant) [37]. Both groups had similar durations of symptoms and peak expiratory flow rates (51%); however, there was a significant difference in treatment. Pregnant women were less likely to be given systemic corticosteroids (44% versus 66%) in the emergency department. This decrease cannot be attributed solely to concern about steroid exposure in the first trimester because the proportion of women who received corticosteroids was similar in all trimesters: 53% first trimester, 40% second trimester, and 50% third trimester. Among those patients who were admitted, pregnant women had significantly lower final peak expiratory flow rate measurements in the emergency department, and had significantly longer hospital stays. On discharge from the emergency department, pregnant patients were significantly less likely to be given systemic corticosteroids ($P=.002$). This undertreatment may explain, in part, the continued asthma symptoms at 2-week

follow-up in pregnant patients (three times more common than in nonpregnant patients; $P=.02$.) Only 41% of pregnant asthmatic women who were seen in the emergency departments were on inhaled corticosteroids when they presented with exacerbations, which is another indication of the undertreatment of asthma in pregnancy [37].

Atopy and allergens

Atopy can contribute to allergic symptoms and asthma when there is seasonal or environmental exposure to specific allergens. Serum IgE or skin prick tests have been used to measure atopy in pregnancy and its effect on asthma [6,32]. Most asthmatic women were atopic in these studies. Stenius-Aarniala and colleagues [32] found that the atopic women had milder asthma, and had significantly fewer hospital admissions than in the nonatopic women. Of the women whose serum IgE increased during their pregnancies, Gluck and Gluck [6] found that asthma remained the same or worsened. In a group of inner city women, Henderson and colleagues [38] found that worsening asthma during pregnancy was associated with increased levels of cockroach-specific IgE. Interactions between pregnancy, atopy, and environmental exposures have not been characterized otherwise in pregnant asthmatic women.

Respiratory tract infections

A decrease in cell-mediated immunity may make the pregnant patient more susceptible to viral infections [39,40]. It was reported that viral infections are the most common precipitators of severe asthma during pregnancy [31]. In addition, sinusitis may exacerbate asthma, and sinusitis was reported to be six times more common in pregnant women compared with nonpregnant women [41].

Pneumonia is found more often in asthmatic women, compared with nonasthmatic women, during pregnancy. Of more than 27,500 pregnant women, 60 had pneumonia during pregnancy [42]. A history of asthma was reported by 37% of this group, compared with 5% in the control group of women who did not have pneumonia and who delivered at the same time. Those who had asthma had a greater than fivefold increased risk for developing pneumonia during pregnancy. These women were more likely to be treated for preterm labor, and delivered at an earlier gestational age [42]. Other studies also found an increased history of asthma (8%–25%) in pregnancies that were complicated by pneumonia [43,44].

Smoking

Smoking is a significant risk factor for adverse pregnancy outcomes, and exacerbates asthma. A survey of new mothers in Australia showed that 21% had a history of asthma and 12% had active asthma. Overall, 22.7% of the women smoked during pregnancy. Current asthmatics were more likely to smoke than

Table 7
Asthma-related health care use by racial group among pregnant asthmatics

Health care outcome	Whites (3030)	Blacks (1285)	Adjusted rate ratio ^a (W/B)
ED visit (11%)	8.7%	16.7%	1:1.89
Rescue CS (12.7%)	11.9%	14.6%	1:1.35
Hospitalized (6.3%)	5.2%	9%	1:1.73

Abbreviations: CS, corticosteroids; ED, emergency department; W/B, white/black.

^a Adjusted for age, education, smoking, high-risk (all $P < .05$).

Data from Carroll KN, Griffin MR, Gebretsadik T, et al. Racial differences in asthma morbidity during pregnancy. *Obstet Gynecol* 2005;106:69.

were nonasthmatics, although this difference was not statistically significant [45]. A review of the data that were collected prospectively from 568 asthmatics did not show an association between smoking and worsening of asthma during pregnancy [13]. This might explain why more asthmatics did not stop smoking during their pregnancies.

Race

A recent study followed 4315 low-income asthmatic women from at least 6 months before pregnancy and through pregnancy. There were 3030 white patients and 1285 black patients; an average of 11% visited the emergency department during pregnancy and 6.3% were hospitalized. Black women were more likely to be treated with corticosteroids (14.6% versus 9% for whites), although their incidence of smoking was much lower than whites (15% versus 50%). After adjusting for age, education, smoking, and high-risk pregnancies, the asthma-specific morbidity in pregnancy was significantly higher in blacks (Table 7) [46].

Summary

The course of asthma is changed by pregnancy in variable ways for unknown reasons. Although the prospective studies used different criteria to stratify the severity of the patients' asthma, their conclusions were remarkably similar. Overall, an equal number of women have asthma symptoms that improve, worsen, or are unchanged through pregnancy. Asthma symptoms can worsen during pregnancy because of identifiable factors, such as infection, gastroesophageal reflux disease, reduction of appropriate medications by physician or patient, and smoking. Undertreatment, which remains a problem during pregnancy, can lead to continued difficulty with asthma.

Severe asthmatics tend to have increased symptoms compared with mild asthmatics. If symptoms worsen, it usually occurs in the second and third trimesters, with the peak in the sixth month. Generally, there is improvement in asthma in the last 4 weeks of pregnancy.

During labor and delivery, only 10% to 20% of asthmatics have symptoms; severe asthmatics are more likely to have exacerbations. Asthma tends to return to the prepregnancy state within 3 months post partum. Successive pregnancies tend to have a similar course in each individual.

Every asthmatic woman should be maintained on appropriate medications and followed carefully throughout pregnancy, especially in the second and third trimesters. Asthma specialists should be available for collaborative care when asthma is uncontrolled, or if there is an exacerbation. A timely adjustment in treatment for any changes in asthma course that might occur ensures the best control of the disease in the face of complex multiple influences.

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