



Asthma in pregnancy: association between the Asthma Control Test and the Global Initiative for Asthma classification and comparisons with spirometry



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ABSTRACT

Objective: The aim of this study was to identify a possible association between the assessment of clinical asthma control using the Asthma Control Test (ACT) and the Global Initiative for Asthma (GINA) classification and to perform comparisons with values of spirometry.

Study design: Through this cross-sectional study, 103 pregnant women with asthma were assessed in the period from October 2010 to October 2013 in the asthma pregnancy clinic at the Clinical Hospital of the Federal University of Pernambuco. Questionnaires concerning the level of asthma control were administered using the Global Initiative for Asthma classification, the Asthma Control Test validated for asthmatic expectant mothers and spirometry; all three methods of assessing asthma control were performed during the same visit between the twenty-first and twenty-seventh weeks of pregnancy.

Results: There was a significant association between clinical asthma control assessment using the Asthma Control Test and the Global Initiative for Asthma classification ($p < 0.001$). There were also significant associations between the results of the subjective instruments of asthma (the GINA classification and the ACT) and evidence of lung function by spirometry.

Conclusions: This study shows that both the Global Initiative for Asthma classification and the Asthma Control Test can be used for asthmatic expectant mothers to assess the clinical control of asthma, especially at the end of the second trimester, which is assumed to be the period of worsening asthma exacerbations during pregnancy. We highlight the importance of the Asthma Control Test as a subjective instrument with easy application, easy interpretation and good reproducibility that does not require spirometry to assess the level of asthma control and can be used in the primary care of asthmatic expectant mothers.

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Introduction

Asthma is likely the most common chronic medical condition during pregnancy, with a worldwide prevalence estimated to be between 8 and 13% [1]. Often identified by dyspnea, asthma can be confused with the physiological dyspnea of pregnancy, but it differs from this condition by presenting with other signs and symptoms, such as cough, wheezing and/or tightness of the

chest [2]. The worsening of asthma symptoms during pregnancy is more common among women who have inadequate control of the disease before pregnancy, and the final period of the second trimester is considered critical for acute exacerbations [3]. Approximately 9–11% of asthmatic pregnant, even those under the care of experts in the treatment of asthma, have acute exacerbations of the disease and require emergency care or hospitalization [4].

Many asthmatic pregnant women consider their asthma to be well-controlled, although they have frequent symptoms that require the physician specifically to question various manifestations of the disease over the course of the pregnancy. Those patients who fail to recognize or do not realize the severity of symptoms are at a higher risk of complications and exacerbations

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of asthma [5]. Several unfavorable obstetric and perinatal outcomes have been described as more frequent among pregnant women who fail to achieve clinical control of asthma, such as pre-eclampsia, prematurity, low birth weight, intrauterine growth restriction, congenital malformations and perinatal death. Given this lack of perception of worsening and the need to maintain clinical control of asthma, spirometry stands out as a tool for diagnosis, evaluation and control of asthma in pregnant women and has an inestimable value of great applicability in clinical practice [6].

The subjective evaluation of unstructured asthma control might fail to distinguish between controlled and uncontrolled patients and lead to insufficient treatment or excessive use of medications [7]. Currently, Asthma Control Questionnaires validated for the Portuguese language are available [5,8]. One of these questionnaires, the Asthma Control Test (ACT), was developed in 2004 by Nathan, can be self-administered and is composed of five items [9]. This instrument is considered a helpful tool in the identification of poorly controlled asthmatic patients during and treatment and follow-up [10]. Recently, the ACT has been used in pregnant women with asthma, and its ability to identify controlled and uncontrolled asthma was validated in the Portuguese language, Brazilian version [11].

The current study aimed to identify a possible association between clinical asthma control as assessed by the ACT and the GINA classification and to compare these with an objective instrument for measuring pulmonary function, spirometry, at the end of the second trimester of gestation, a period considered to be the time of the highest risk of clinical worsening and exacerbations of asthma. This study was carried out in the Brazilian outpatient asthma pregnancy clinic, where obstetrical and pulmonary specialists work together in a pioneering way to create an environment that is favorable for the most efficient and appropriate diagnosis and treatment of these women.

Materials and methods

This was a cross-sectional study involving 103 asthmatic pregnant women who were assessed in the period from October 2010 to October 2013 in the asthma pregnancy clinic at the Clinical Hospital of the Federal University of Pernambuco. These patients had a previous diagnosis of asthma and were referred to the asthma clinic from the same hospital or from other hospitals. The inclusion criteria were: single pregnancy, diagnosis of asthma prior to pregnancy, early prenatal care from the 6th week of pregnancy and completion of at least one clinical control assessment by the GINA classification, ACT and spirometry, at the same time, during the period between the twenty-first and the twenty-seventh weeks of pregnancy. While carrying out the examinations, each patient had no knowledge of the results and was only given results after the conclusion of the three exams in order not to influence (by overestimating or underestimating) the responses to the questionnaire (Fig. 1). The exclusion criteria were: lung diseases

other than asthma, heart disease or anatomical alterations of the chest, inability to provide information properly or attend consultations due to intellectual or cognitive difficulty, current participation in a test or any other clinical intervention study and intention of abortion.

Clinical factors

Data related to the frequency of symptoms (number of days with no asthma symptoms, number of nights that asthma interfered with sleep, number of days that asthma interfered with usual activities) were obtained at monthly visits.

To confirm pregnancy, positive β -human chorionic gonadotropin (β -hCG) and obstetric ultrasound examination were used. The diagnosis of asthma during pregnancy was substantiated by the presence of one or more symptoms of dyspnea, chronic cough, wheezing, tightness in the chest or thoracic discomfort, particularly at night or in the early morning hours; episodic symptoms; spontaneous improvement with the use of specific medications for asthma (bronchodilators, corticosteroids); three or more episodes of wheezing in the last year; seasonal variability of symptoms and positive family history of asthma or atopy. The diagnosis of asthma was confirmed by the identification of reversible airflow limitation by pulmonary function test results such as the spirometric finding of obstructive airways characterized by reduced forced expiratory volume in the first second (FEV₁) below 80% predicted and its relation to forced vital capacity (FVC) below 75% in adults or airflow obstruction, which disappears or improves significantly after bronchodilator use [12]. Asthmatic pregnant women with a report and/or referral from a pulmonologist, regardless of the presence of symptoms in the last year, were considered. Asthma in pregnancy was classified as intermittent, mild persistent, moderate or severe, as adapted from the National Heart, Lung, and Blood Institute [13].

The treatment of asthma during pregnancy included no treatment, use of short-acting beta-agonists, short-acting beta-agonists and inhaled corticosteroids (ICS), and ICS and long-acting beta-agonists (LABA). At the end of the second trimester of pregnancy, after having undergone consultations in the asthma clinic, asthma control was classified as controlled, partially controlled and uncontrolled according to the GINA classification [12]. The information related to symptom frequency (number of days with no asthma symptoms, number of nights that asthma interfered with sleep, number of days that asthma interfered with usual activities) was obtained at monthly visits. The two categories of the validated ACT controlled asthma and uncontrolled asthma were considered to correspond to partially controlled and uncontrolled asthma (GINA, 2010).

The ACT has already been validated among pregnant women, with the following classifications: controlled (≥ 16 points) and uncontrolled (< 16 points) (Fig. 2). The most accurate cut-off point was 16, with a sensitivity of 95.4%, specificity of 68.8%, negative predictive value of 91.7% and positive predictive value of 80.5%. The positive and negative likelihood ratios were 3.052 and 0.067, respectively. The questionnaire was found to be highly effective for discriminating between controlled and uncontrolled asthma, with an area under the receiver operating characteristic (ROC) curve of 0.846 (95% CI: 0.74–0.92) [11].

This study was approved by the Ethics Committee of the Federal University of Pernambuco with the CAEE 27133914.0.0000.5208. Written informed consent was obtained from the pregnant women with asthma who were enrolled in the study, and written permission from parents and/or caregivers was obtained for asthmatic pregnant women aged < 18 years.

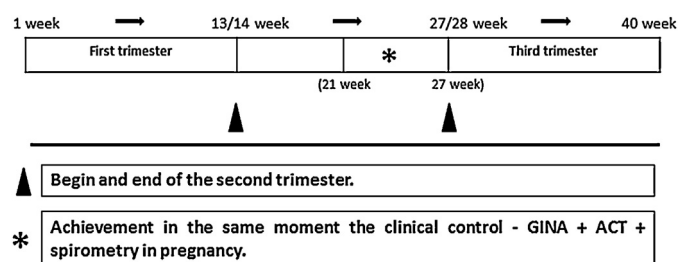


Fig. 1. Flowchart of the clinical exams and clinical attendance for asthmatic expectant mothers.

Criteria / Score	1	2	3	4	5
In the last 4 weeks, how long did your asthma put you away from your activities?	At all times	Most of the time	Sometimes	Rarely	Never
In the last 4 weeks, which was the frequency of occurrence of tiredness?	Once a day	Once a day	Three to six times per week	One to two times per week	Rare
In the last 4 weeks, how often did you have nocturnal awakenings with asthma symptoms?	Four or more nights per week	Two to three nights per week	Once a week	Once or twice	Never
In the last 4 weeks, how often did you usage of inhaled medication or nebulization?	Three or more times per day	One to two times per day	Three to six times per week	Once a week or less	Never
In the last 4 weeks, how would you rate the asthma control?	Uncontrolled	Poorly controlled	Moderate level of control	Well controlled	Completely controlled

Fig. 2. Asthma Control Test (ACT): controlled (≥ 16 points) and uncontrolled (< 16 points).

Source: Roxo et al. [8].

Statistics and data analysis

The demographic data of asthmatic expectant mothers are presented in tabular form with their corresponding relative and absolute frequencies. Numerical variables are represented by the measures of central tendency and dispersion measurements. In the analysis of the existence of association, the chi-square test was used for categorical variables. For the quantitative variables, the Kolmogorov–Smirnov test for normality was used. Comparison between two different groups was performed by Student's test (normal distribution) and the Mann–Whitney test (non-normal distribution). Comparison of more than two groups was performed by ANOVA (normal distribution) and the Kruskal–Wallis test (non-normal distribution). A 95% confidence interval (CI) was used for all tests. STATA/SE 12.0 and Excel 2010 were used for statistical software.

Results

Data from 103 pregnant women with asthma who were assessed in the asthma pregnancy clinic at the Hospital das Clínicas – UFPE were analyzed. Seventy-nine (76.7%) patients were in the 18–34 year old age group. Analysing the initial care of these patients, 50 (48.5%) patients were in early pregnancy (< 20 weeks), and 50 (48.5%) patients had a high body mass and were considered overweight. Among the 62 expectant mother asthmatics, 60.2% were taking short-acting inhaled beta-agonist (salbutamol or fenoterol), and during exacerbations, inhaled corticosteroids (budesonide, beclomethasone or fluticasone) at doses between 400 and 800 μg per day. Among the most frequent comorbidities, hypertension and gestational diabetes were the most common, and all 47 (45.6%) patients with other atopic diseases had rhinitis (see Table 1).

Based on the evaluation of the classification of asthma and its clinical control in the period between the twenty-first and twenty-seventh weeks of gestation, mild persistent asthma was most frequent, and the percentage of pregnant women with partially controlled and uncontrolled asthma was the same (Table 2).

There was an association between asthma control by the Global Initiative for Asthma (GINA) classification and the Asthma Control Test (ACT) in pregnancy, with $p < 0.001$ (95% CI) among expectant mothers who were being evaluated in the period between the twenty-first and the twenty-seventh weeks of gestation (Table 3).

Analysing the subjective instruments of asthma control (GINA and the ACT) and the results of pulmonary function testing by spirometry, we found $p = 0.002$ when comparing the FVC to the

ACT and $p < 0.001$ when comparing FEV₁ to ACT. Comparing FVC, FEV₁ and FEV₁/FVC with the clinical control determined by the GINA classification, we found $p = 0.003$, $p < 0.001$ and $p = 0.001$, respectively (Table 4).

Table 1

Demographic characteristics of 103 asthmatics expectant mothers.

Variables	N	%
Age		
<18 years old	13	12.6
18–34 years old	79	76.7
≥ 35 years old	11	10.7
Education level		
First degree	32	31.1
High school	64	62.1
Complete or incomplete graduation	7	6.8
IG		
<20 weeks	50	48.5
20–26 weeks	37	35.9
≥ 27 weeks	16	15.6
IMC		
Underweight	2	1.9
Normal weight	36	35.0
Overweight	50	48.5
Obese	15	14.6
Treatment		
None	16	15.5
Short-acting beta-agonist	14	13.6
Short-acting beta-agonist + IC ^a	62	60.2
IC + LABA ^b	11	10.7
Smoking		
Yes	9	8.7
No	94	91.3
Alcoholism		
Yes	2	1.9
No	101	98.1
Comorbidities		
Yes – TOTAL	(23)	22.3
Gestational hypertension	12	
Gestational diabetes	5	
Others	6	
No	(80)	77.7
Associated atopy		
Yes – TOTAL	(47)	45.6
Rhinitis	47	
No	(56)	54.4

^a IC, inhaled corticosteroid.

^b LABA, long-acting beta agonist.

Table 2

Clinical data of 103 asthmatic expectant women assessed between the twenty-first and twenty-seventh weeks of gestation.

Variables	N	%
Asthma classification		
Intermittent	31	30.1
Mild persistent	51	49.5
Moderate persistent	13	12.6
Severe persistent	8	7.8
Asthma control – GINA classification		
Uncontrolled	8	11.2
Partially controlled	32	44.4
Controlled	32	44.4
Not applicable (intermittent)	31	–

Table 3

Association between asthma control by the GINA classification and the Asthma Control Test (ACT) in 103 asthmatic expectant mothers between the twenty-first and twenty-seventh weeks of gestation.

Asthma Control Test (ACT)	Global Initiative for Asthma (GINA) classification			p-Value ^a
	Controlled N (%)	Partially controlled N (%)	Uncontrolled N (%)	
Controlled	32 (57.1)	23 (41.1)	1 (1.8)	<0.001
Uncontrolled	0 (0.0)	9 (56.2)	7 (43.8)	

^a Chi-square test.

Comments

To the best of our knowledge, this is the first study to evaluate the association between clinical asthma control by the Asthma Control Test (ACT) in pregnancy and the Global Initiative for Asthma (GINA) classification and to compare an objective instrument for measuring pulmonary function – spirometry – with two subjective instruments for the clinical evaluation of asthma during late second trimester pregnancy [11,12]. In this study, there was a statistically significant association between the clinical control of asthma during pregnancy by the GINA classification and the ACT, with $p < 0.001$. Significant associations were also found when comparing ACT with FVC ($p = 0.002$) and FEV₁ ($p < 0.001$). These important results enable physicians to use any one of the instruments of clinical follow-up during a period considered to be the highest risk of worsening clinical condition and exacerbation of asthma during pregnancy [3,14,15].

Table 4

Comparison of spirometry, the Asthma Control Test (ACT) in pregnancy and clinical control by the GINA classification in 103 asthmatics expectants mothers at the same time, in the period between the twenty-first and twenty-seventh weeks of gestation.

Variables	Spirometry		
	FVC Average ± DP	FEV ₁ Average ± DP	FEV ₁ /FVC Average ± DP
ACT			
Controlled	83.95 ± 11.65	80.96 ± 13.03	81.27 ± 9.43
Uncontrolled	73.97 ± 10.91	67.11 ± 15.84	74.88 ± 14.61
p-Value	0.002 ^a	<0.001 ^a	0.134 ^b
Control GINA			
Controlled	85.57 ± 10.37	83.90 ± 11.60	84.20 ± 5.56
Partially controlled	77.91 ± 9.57	71.06 ± 10.37	74.86 ± 11.40
Uncontrolled	75.15 ± 8.48	66.49 ± 14.54	70.71 ± 11.91
p-Value	0.003 ^c	<0.001 ^c	0.001 ^d

^a Student's test.

^b Mann–Whitney test.

^c ANOVA.

^d Kruskal–Wallis test.

Dyspnea during pregnancy can be considered physiologic, but when it is accompanied by others signs and symptoms, such as cough, wheezing or tightness of the chest with shortness of breath, it suggests a diagnosis of asthma. In this research context, spirometry and peak expiratory flow (PEF) are important objective tools to diagnose asthma and monitor pulmonary function during pregnancy and are not essentially affected by this condition; they have thus become indications in a routine medical evaluation [16–20].

Several self-administered standardized questionnaires, such as the Asthma Control Test (ACT) and the Asthma Control Questionnaire (ACQ), can be applied. These questionnaires are simple and can be utilized by health professionals in order to assess asthma control. The ACT contains five questions that are related to the frequency of the symptoms of asthma and need for using rescue medication during the previous 4 weeks. The scores are expressed in numerical values and reflect asthma control, ranging from an ACT score of 5 (worse control) to 25 (total control) [9]. It was specifically engineered for use in clinical practice and has some important points of its use: first, by not requiring the evaluation of pulmonary function, the ACT provides a simpler evaluation of control than the ACQ. Therefore, it is more useful and practical and can be used in primary care settings. Second, the ACT is a useful tool that allows for the adjustment (step-up or step-down) of asthma treatment regimens on the basis of pre-specified cut points. Third, the ACT is suitable for periodic monitoring of patients with asthma because it can be administered by mail, in pharmacies, over the Internet and by telephone.

The stage of pregnancy can have a significant impact on asthma symptoms, with many pregnant women noticing a worsening peak late in the second trimester and a return to pre-pregnancy symptoms 3 months after delivery [15,21]. During pregnancy, approximately 5.8% of patients are hospitalized for asthma exacerbations [22], with some studies have shown that more than 20% of women with exacerbations require intervention, including hospitalizations, unscheduled visits to the doctor and emergency care [23,24]. Pregnant women with mild persistent asthma had an exacerbation rate of 12.6% and a hospitalization rate of 2.3%; with moderate persistent asthma, the exacerbation rate was 25.7% and the hospitalization rate was 6.8%, and with severe persistent asthma, the exacerbation rate was 51.9% and the hospitalization rate was 26.9% [23]. The risk factors that can trigger and worsen asthma exacerbations in pregnancy include: inadequate antenatal care, obesity, smoking, lack of adherence to asthma treatment or suspension of control medications without medical guidance, atopy, respiratory infections, sinusitis, gastro-esophageal reflux and emotional disturbances [3,15,16,25–27].

Obesity is associated with an increased risk of asthma exacerbation during pregnancy and also with high risks of non-pulmonary complications, including pre-eclampsia, gestational diabetes and hypertension of pregnancy [26]. For smoking, only nine (8.7%) of the expectant mothers continued actively smoking, despite anti-smoking warning programs, which were offered to all asthmatic expectant mothers and included guidance for avoiding passive smoke exposure.

The goal of asthma treatment during pregnancy is the same as for asthma in general, including the prevention of severe exacerbations, improvement in quality of life and maintaining normal pulmonary function [12,13,16]. The use of inhaled corticosteroids has been shown to reduce the occurrence of exacerbations during pregnancy and decrease the rate of hospital admissions for asthma [15]. Despite these data, retrospective reviews of the care of asthma has shown that the use of inhaled corticosteroids in pregnant women with asthma decreases 22–35% after the diagnosis of pregnancy [27–31], probably due to lack of the understanding of safety of these medications during pregnancy

[32]. Conversely, the safety of treatment with long-acting beta-2 agonists during pregnancy requires further investigation, as does the use of corticosteroids in high doses. The impact of asthma, especially when poorly controlled, which increases the risk of adverse outcomes in pregnancy, might be more pronounced than the potential negative effects provoked by these drugs [33,34].

This study shows that assessment of the clinical control of asthma in the expectant mother can be performed with both the ACT and the GINA classification. We highlight the importance of the ACT as a subjective instrument with easy application, easy interpretation and good reproducibility that does not require spirometry to assess the level of asthma control in pregnancy. The ACT, the GINA classification or spirometry can be used to evaluate the level of asthma control in pregnant women during the period between the twenty-first and twenty-seventh weeks of pregnancy.

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Conflict of interest

The authors report no conflict of interest.

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