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Validation of the Asthma Control Test in pregnant asthmatic women

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KEYWORDS

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Summary

Objective: To determine the validity of the Asthma Control Test (ACT) questionnaire for assessing pregnant asthmatic women.

Methods: The study involved 40 pregnant asthmatic women over a total of 113 medical visits. On each occasion the participants had a pulmonary function test and a clinical evaluation to assess the level of asthma control. In addition, the ACT was carried out with the obstetrician being blinded to its results.

Results: The most accurate cut-off point was 16, with a sensitivity of 95.4%, specificity of 68.8%, a negative predictive value of 91.7% and a 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: 0.748–0.92). Reliability assessed in patients with the same clinical classification resulted in an intra-class correlation coefficient of 0.86 (95%CI: 0.75–0.93). Improved clinical conditions corresponded to a significant increase in the ACT score ($p < 0.005$), indicating good responsiveness to changes in clinical status.

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Conclusions: The ACT proved to be reliable and could discriminate between levels of asthma control in pregnant women confirming its value as a useful tool for the management of asthma during pregnancy.

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Introduction

Asthma is characterized by an increase in airway sensitivity and chronic inflammation leading to an obstruction that is partially or completely reversible [1]. It is the most common chronic disease in women of reproductive age [2], affecting up to 8% of pregnant women in the United States [3].

The course of asthma in pregnant woman is unpredictable. Improvement is observed in one-third of cases, deterioration in another third and no change in the remainder [4]. Pregnant asthmatic women are at an increased risk of experiencing preeclampsia, premature delivery, intrauterine growth restriction, and of being submitted for cesarean section [1,5]. Furthermore, asthmatic exacerbations during pregnancy are associated with an increased risk of congenital malformations [6]. However, when well-controlled, asthma is associated with a good fetal and maternal prognosis [7]. Therefore, keeping the disease under control is pivotal for an uneventful pregnancy and a healthy newborn infant [8].

A subjective evaluation of asthma control can be of no assistance in distinguishing between well-controlled and uncontrolled patients, leading either to insufficient treatment or to excessive medication [9,10]. In pregnant women, shortness of breath is the most common respiratory complaint. However, this physiological dyspnea is not associated with the other typical symptoms of asthma such as wheezing, coughing and chest tightness [11,12]. Thus obstetricians unfamiliar with the disease may find it difficult to evaluate the level of asthma control in pregnant women due to the numerous peculiarities and complaints produced by pregnancy itself.

The ACT questionnaire was developed in 2004 by Nathan et al. [13] and can be self-administered. It can be used for identifying patients with poorly controlled asthma and for monitoring treatment [14]. It has been validated in Spain [15], China [16], Korea [17], North Africa [18], Brazil [19], Greece [20], Vietnam [21] and Turkey [22]. Some authors have recommended its use to evaluate pregnant women [23].

However, to the best of our knowledge, no studies have assessed ACT's performance in pregnant asthmatic women and it is not known to what extent the presence of the breathlessness due to pregnancy itself may alter the value of the ACT score. Thus the objective of the present study was to assess the ability of the ACT questionnaire to distinguish between pregnant women with controlled asthma from those with poorly controlled disease and verify its reliability and responsiveness.

Patients and methods

A convenience sample of forty pregnant women was recruited from consecutive patients seeking care at the

sub-specialty outpatient department for asthma in pregnancy located at the Hospital das Clínicas, the teaching hospital at the Federal University of Pernambuco (UFPE), Brazil, between December 2011 and October 2012. The women were 18 years of age or more, of more than 12 weeks in gestational age and had had a positive diagnosis for asthma. The study was approved by the institutional ethics committee and all patients signed an informed consent form.

A validation study was chosen as the most appropriate study design. Evaluations were conducted prior to delivery over a maximum of four visits scheduled at least four weeks apart. At each visit, the patients answered the Portuguese version of the ACT questionnaire [19], while a single obstetrician trained in the management of pregnant women with asthma performed a clinical evaluation and spirometry. Asthma diagnosis was confirmed by the clinical history and a previous increase of more than 12% in the one-second forced expiratory volume (FEV₁) after bronchodilation [24].

The first procedure at each visit was the pulmonary function test conducted using spirometry. The variable FEV₁, expressed as a percentage of the predicted value, was the parameter used to evaluate the degree of airway obstruction. Next, the ACT questionnaire was completed. Since there was no restriction in the study protocol on the inclusion of individuals with little or no schooling, the questionnaire was applied by interviewers, who had been instructed not to interpret the questions or influence the patients' answers. The pregnant women were asked to refer to their experiences with asthma during the previous four weeks and to answer the questions on the form.

At the end of each visit there was a clinical evaluation in accordance with the Global Initiative for Asthma (GINA) guidelines [24], which, in association with the pulmonary function test results, is considered the gold standard for asthma control. The obstetrician conducting these evaluations had specific training in asthma diagnosis during pregnancy and was blinded to the results of the ACT. At the first visit, clinical examination confirmed the diagnosis of asthma, evaluated its severity and classified the control level of the disease in accordance with the criteria proposed in the GINA guidelines [24]. At the following visits, the procedures consisted of evaluating the level of asthma control during the preceding four weeks.

Based on the GINA criteria, the patients were divided into controlled and uncontrolled asthma groups – the latter including partially controlled and uncontrolled cases. To evaluate the capacity of the ACT to distinguish between controlled and uncontrolled asthma, the patients were classified based on a score that ranged from 5 to 25. Validation measures were applied for each of the scores – sensitivity, specificity, positive and negative predictive

values and likelihood ratios – obtained in the diagnostic test.

Accuracy was determined from the area under the receiver operating characteristic (ROC) curve and used to calculate the proportion of patients who had been correctly classified by the questionnaire. The intra-class correlation coefficient was used to assess reliability for patients maintaining the same level of control over more than one visit. The Wilcoxon test was used to evaluate responsiveness according to variations in the ACT scores of the patients whose clinical status changed between two evaluations. The statistical analyses were conducted using the Stata software program, version 12.1SE and the EpiInfo program, version 3.04.

Results

The initial study sample consisted of 40 pregnant women. There was a cumulative loss-to-follow-up during subsequent visits and asthma control assessment was based on 113 evaluations. The median age of the women was 24 years (range 18–44 years), median family income was 387 dollars, and slightly more than half the participants (57.5%; $n = 23$) had between 9 and 11 years of schooling. FEV₁ was >80% of the predicted value in 67 evaluations (59.3%). Three of the forty women (7.5%) reported smoking. Allergy was reported by 30 women (75%) and rhinitis by 19 (47.5%), while 37 of the 40 participants (92.5%) reported having a previous diagnosis of asthma. In accordance with the asthma severity classification, 27.5% of the women in the study had intermittent asthma, while 15% had mild persistent, 30% moderate persistent and 27.5% severe persistent asthma (Table 1).

Table 2 shows the values for sensitivity, specificity, positive and negative predictive values and likelihood ratios for the various ACT scores. The highest accuracy of the ACT score distinguishing controlled from uncontrolled asthma was found with a cut-off value of 16 points (84%), with high sensitivity (95.4%) and high negative (91.7%) and positive predictive (80.5%) values. Specificity was 68.8%, the positive likelihood ratio was 3.05 and the negative likelihood ratio was 0.067. The area under the ROC curve was 0.846 (95% CI: 0.748–0.920) (Fig. 1).

The intra-class correlation coefficient was 0.86 (95% CI: 0.75–0.93). This variable provides a measurement for the level of control of the patients who remained stable between two or more clinical evaluations. In order to evaluate responsiveness the questionnaires of 10 patients whose clinical condition improved from poorly controlled to controlled between one clinical evaluation and another were assessed. The median ACT score was 11 points (range 9–14) in patients with poorly controlled asthma and 20.5 points (range 18–24) in those whose clinical classification improved ($p < 0.005$) indicating that the questionnaire can detect clinical change (Fig. 2).

Discussion

To the best of our knowledge, this is the first study to evaluate prospectively the ACT reliability in identifying uncontrolled asthma and its responsiveness to treatment in

Table 1 Characteristics of the pregnant women enrolled to the study.

Characteristic	Number of women
<i>Number of participants at:</i>	
First visit	40
Second visit	33
Third visit	27
Fourth visit	13
Median age (Range) in years	24 (18–44)
Family income in US dollar (median – P ₂₅ ; P ₇₅)	387 (264; 575)
<i>Years of schooling</i>	
1–8	14 (35.0%)
9–11	23 (57.5%)
≥12	03 (7.5%)
<i>Classification of severity</i>	
Intermittent	11 (27.5%)
Mild persistent	06 (15.0%)
Moderate persistent	12 (30.0%)
Severe persistent	11 (27.5%)
<i>FEV₁ (First visit/total)</i>	
<60%	7 (17.5%)/12 (10.6%)
60–79%	18 (45%)/34 (30%)
>80%	15 (37.5%)/67 (59.3%)
<i>Comorbidities</i>	
Smoking	03 (7.5%)
Allergy	30 (75.0%)
Rhinitis	19 (47.5%)
Previous diagnosis of asthma	37 (92.5%)

pregnant women. The results show that a test score of 16 resulted in the highest accuracy for distinguishing controlled from uncontrolled disease. The sensitivity, predictive positive and negative values and likelihood ratios were similar to those found by others in non-pregnant patients [13–22].

However, the specificity of the ACT was slightly lower (68.8%) but also comparable with that found in non-pregnant patients (70.8–78.5%) [13–22]. This finding could be also a consequence of the pregnancy on symptoms perception by the patients and should call some caution to its applicability as a diagnostic confirmation test of adequate control of the disease. However, the ACT questionnaire should still be used as a screening tool because in an un-specialized office it is more important to identify patients that need of asthma care. In this situation the benefits of high sensitivity more than offset the slight loss in specificity.

Although our findings indicate that a cut-off point of 16 provides the best accuracy for distinguishing controlled from uncontrolled asthma, when our results are compared to those of Schatz et al. [14], we can conclude that a cut-off point of 19 also shows a good balance between sensitivity (86%) and specificity (75%) for detecting patients with partially controlled disease (Table 2) and should call attention as an indication of asthma control problems.

The good responsiveness found shows that the ACT was able to identify changes in asthma control in patients who

Table 2 Characteristics of the ACT questionnaire applied to the pregnant women.

Cut-off point (ACT score)	Sensitivity (%)	Specificity (%)	Accuracy (%)	Likelihood ratio		PPV (%)	NPV (%)
				Positive	Negative		
7	100	0	57.5	1	.	57.5	100
8	100	4.2	59.3	1.043	0	58.6	100
9	100	12.5	62.8	1.143	0	60.7	100
10	100	18.8	65.5	1.231	0	62.5	100
11	100	27.1	69.0	1.371	0	65.0	100
12	100	33.3	71.7	1.500	0	67.0	100
13	100	41.7	75.2	1.714	0	69.9	100
14	98.5	47.9	77.0	1.890	0.032	71.9	95.8
15	98.5	60.4	82.3	2.487	0.025	77.1	96.7
16	95.4	68.8	84.1	3.052	0.067	80.5	91.7
17	92.3	70.8	83.2	3.165	0.109	81.1	87.2
18	90.8	70.8	82.3	3.165	0.109	80.8	85
19	86.2	75.0	81.4	3.446	0.185	82.4	80
20	76.9	77.1	77.0	3.357	0.299	82.0	71.2
21	67.7	87.5	76.1	5.415	0.369	88.0	66.7
22	61.5	87.5	72.6	5.415	0.369	87.0	62.7
23	52.3	87.5	67.3	5.415	0.369	85.0	57.5
24	30.8	93.8	57.5	4.923	0.738	87.0	50
25	10.8	97.9	47.8	5.169	0.911	87.5	44.8

PPV: positive predictive value; NPV: negative predictive value.

experienced a clinical improvement during follow-up. This result is similar to those found with the Portuguese, Turkish and Spanish versions [19,22,15].

The reliability of the ACT questionnaire was high, with an intra-class correlation coefficient of 0.86, a value that is higher than that reported for the original version of the test [13].

Although the ACT was constructed as a self-answered questionnaire, in the present study it was applied by

interviewers in order to homogenize procedures and avoid bias. Although this could be seen as a caveat for its general acceptability, the training of the health allied professionals that obtained the answers posed no difficulties and completion of questionnaire answering was in less than 5 min.

In a busy primary obstetric practice, the answers to the questionnaire can be obtained by an easily trained health allied professional, especially for patients with little schooling or language difficulties, saving time for the physician and offering a rapid evaluation of asthma control status, allowing better decisions for therapeutics changes and follow-up of disease control.

Together these results show that the ACT is a simple but accurate tool for evaluating asthma control in pregnancy

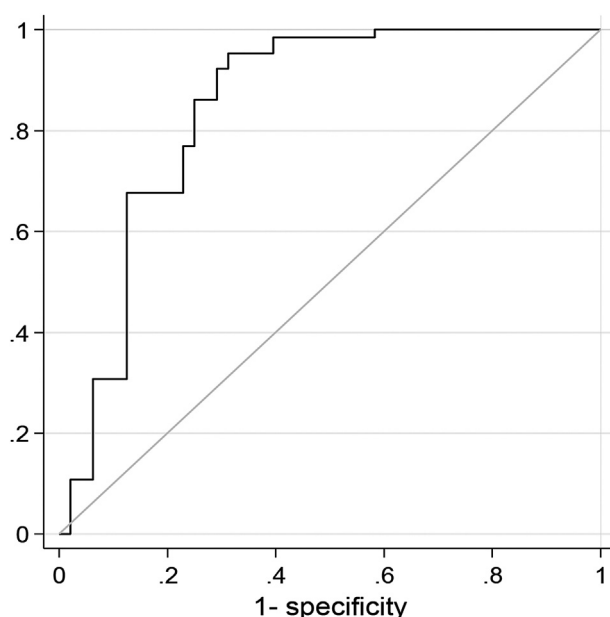


Figure 1 ROC curve for the ability of the ACT to identify patients with uncontrolled asthma. Area under the curve = 0.846 (95% CI: 0.748–0.920).

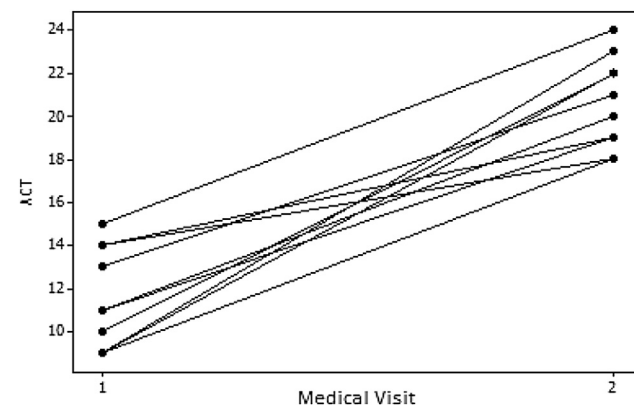


Figure 2 Responsiveness of the ACT questionnaire to improvement in symptoms in treated patients evaluated at two separate visits ($p < 0.005$).

with the ability to identify those women in need of specialist intervention.

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Conflict of interest

All authors have no conflict of interest.

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