

A Study of Correlation between Asthma Control Test and Lung Function Parameters

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ABSTRACT

Introduction: Asthma control is the extent of observed asthma symptoms in patients and reduction in symptoms after treatment. Simple screening tools are available to assess asthma control. Asthma control test is a simple numerical scoring system that can be easily used on a routine basis. Latest Global Initiative for Asthma (GINA) guidelines stress that asthma control is the main objective of asthma treatment. In this COVID-19 pandemic situation, there is an hesitancy in performing and undergoing pulmonary function tests among physicians and the patients. Hence, in this study it was planned to correlate the asthma control test values with FEV1 and other parameters like Peak Expiratory Flow Rate (PEFR), Absolute Eosinophil Count (AEC) and serum magnesium.

Aim: To study the correlation between asthma control test and FEV1; to study the correlation between asthma control test and other parameters like PEFR, AEC and Serum magnesium.

Materials and Methods: This was a cross-sectional observational study done from February 2019 to January 2020 conducted at Department of Pulmonary Medicine. A total of 55 patients of

Bronchial asthma in line with GINA Guidelines were included in the study. Asthma control test questionnaire was administered to all the patients. Routine blood investigations like Total Leucocyte Count (TLC), Differential Leucocyte Count (DLC), Absolute Eosinophil Count (AEC), serum magnesium levels were done. Pulmonary function parameters like FEV1 and PEFR were measured.

Results: Asthma control test had positive correlation with FEV1 with a spearman's correlation of 0.2758 and p-value of 0.0414 which was statistically significant. The spearman's correlation between asthma control test and AEC was -0.4583 with a p-value of <0.001, which was significant. The correlation of asthma control test with serum magnesium was 0.3414 with a p-value of 0.010.

Conclusion: Asthma control test score had a significant positive correlation with FEV1 and serum magnesium levels. It also had significant negative correlation with AEC (inflammatory marker). Hence, asthma control test can be used as tool for treatment response in the current COVID-19 pandemic situation and also in resource limited settings.

Keywords: Absolute eosinophil count, Forced expiratory volume, Peak expiratory flow rate, Serum magnesium

INTRODUCTION

Bronchial asthma is one of the most common chronic airway diseases characterised by hyper responsiveness of airways and reversibility in bronchoconstriction after nebulisation with bronchodilator. Bronchial asthma affects 1-18% of population in different countries [1].

Asthma control is the extent of observed asthma symptoms in patients and reduction in symptoms after treatment. Asthma control have two domains i.e., symptom control and future risk of exacerbations. Simple screening tools are available to assess asthma control. Various tools available are GINA symptom control tool, primary care asthma control tool. There are a few numerical asthma control tools which scores and cuts points to distinguish different symptoms and severity of asthma [1].

Asthma severity is assessed retrospectively based on the level of treatment required for symptom control and prevention of exacerbations. Mild asthma is asthma that is well controlled with step 1 and step 2 of treatment, moderate asthma is asthma controlled with step 3 of treatment and severe asthma is asthma controlled by step 4 and step 5 of treatment [1,2].

Poor asthma control leads to substantial effect on quality of life and economic burden. Various host factors and environmental factors are responsible for development and control of bronchial asthma. Host factors are genetics, obesity, sex and preterm or with small size for gestational age. Environmental factors are allergens, infections, microbiome, occupational sensitizers, microbiome, diet, stress and smoking [1,3].

Numerical asthma control tools available are asthma control questionnaire and asthma control test. Asthma control questionnaire

score ranges from 0-6, higher the value, worse is the asthma control. Asthma control test scores range from 5-25, higher the value, better is the asthma control [1].

ACTs have good accuracy for screening control of asthma. An ACT score of 19 or less suggests patients might be experiencing control problems. This score detected severe asthma with specificity (71%) and sensitivity (71%). A score of 19 or less might obviate the need for further evaluation of the patient to determine measures required to improve asthma control. The data from different studies suggests that a score of 16 or less is of concern because it predicts poor control of asthma [2].

Schatz M et al., performed a study on reliability of asthma control test which showed it was reliable and valid in asthma control assessment for patients under the care of asthma specialists. Study also provided evidence that ACT scores change overtime with asthma treatment. Study also observed that ACT correlates poorly with FEV1 which is consistent with the previous studies that concluded asthma control cannot be inferred from single measure of lung function [2].

Lung function should be assessed at diagnosis and three to six months of controlled treatment and periodically thereafter. Studies have shown that FEV1 does not strongly correlate with asthma symptoms in adults and children. PEFR is used as a monitoring tool in asthmatics to predict exacerbation and decline in lung function but the correlation of PEFR with asthma control test has not been studied [4]. Eosinophils have been viewed as the primary effector cell in asthma since their discovery [5]. Various studies have noted that levels of eosinophils in blood is related to disease severity in asthma patients [6,7].

Magnesium is the fourth most common cation in the body. Magnesium has many functions in the body. It competes with calcium influx in the smooth muscles and prevents muscular contraction, stabilises the mast cells, also influences cholinergic transmission and stimulates synthesis of nitric oxide. Both intravenous and nebulised magnesium sulphate are shown to be useful in management of bronchial asthma and the prevalence of hypomagnesemia in bronchial asthma cases is well documented [8].

Many cross-sectional studies have concluded that higher intake of dietary magnesium is associated with decreased airway responsiveness and symptoms in adults. Magnesium has bronchodilator property and this has led to its use for acute asthma exacerbation in emergency department [9].

Asthma control test is a simple numerical scoring system that can be easily used on a routine basis. Latest GINA guidelines stress that asthma control is the main objective of asthma treatment. The objective measures of asthma control include pulmonary function tests measuring FEV₁, PEF_R. The association of AEC and serum magnesium in asthma control has also been studied. But however, literature on correlation of lung function parameters and serum magnesium levels with Asthma control test is limited [1].

In this COVID-19 pandemic situation there is hesitancy in performing and undergoing pulmonary function tests among physicians and the patients. Hence, this study was planned to correlate the asthma control test values with FEV₁ and PEF_R as the primary objective and to correlate the asthma control test with AEC, serum magnesium as secondary objective.

MATERIALS AND METHODS

Study design: A cross-sectional observational study was conducted at Department of Pulmonary Medicine, from February 2019 to January 2020. Ethical clearance was taken from the institutional ethics committee and the ethical clearance number was 1611/IEC/2019. All procedures followed were in accordance with the ethical standards of the committee on human experimentation. Informed consent was obtained from all patients for being included in the study.

Patients of Bronchial Asthma in line with GINA Guidelines were included in the study. Sample size=55 $\{n=(z_{1-\alpha/2})^2(p)(q)/(d)^2\}$ p=Prevalence of asthma in India 3.7% [10].

Each patient was explained in detail about the study and was asked to sign a written informed consent document before enrolment and before any study procedures is performed.

Inclusion criteria: Age more than 18 years, patients diagnosed with asthma according to the current GINA guidelines, mild to moderate asthmatics.

Exclusion criteria: Pregnancy, patients on diuretic therapy, cardiac disease, chronic kidney disease, life threatening asthma, chronic persistent severe asthma.

Asthma Control Test

Asthma control test is a simple numerical tool to assess asthma control which has various parameters like symptom control, frequency of night symptoms, use of controller medications, disturbance from work. It has a total of five questions with a score of 0-5, 0 being the least score and 5 being the highest score in each question. Asthma control test is divided into three categories: well controlled if it 20-25, not well controlled if it is 16-19 and very poorly controlled asthma if less than 15.

A detailed clinical history was taken and a thorough physical examination was done on all the patients included in study. Asthma control test questionnaire was administered to all the patients. Routine blood investigations like TLC, DLC, AEC, serum magnesium levels were done. Pulmonary function parameters like FEV₁ and PEF_R were measured.

STATISTICAL ANALYSIS

Descriptive analysis was done in Microsoft excel software. Statistical tests used for standard deviation and spearman's rank correlation and p-value was calculated to know the significance of correlation.

RESULTS

A total of 55 diagnosed asthma patients were included in the study. The mean age of patients in the study population was 39.9±14.9. A total of 27 females and 28 males were present in the study.

Asthma control test: The mean ACT score was 15.6±4.01. Eight patients had well controlled asthma, 21 patients had partially controlled asthma and 26 patients had uncontrolled asthma [Table/Fig-1].

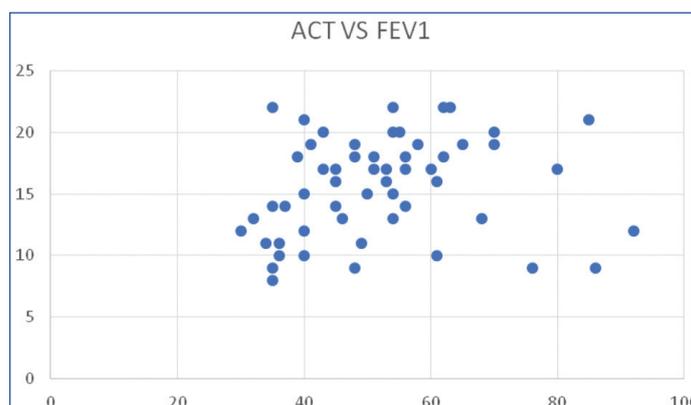
ACT score	Number of patients
0-15 (very poorly controlled asthma)	26 (47%)
16-19 (not well controlled)	21 (38%)
>20 (well controlled)	8 (14%)

[Table/Fig-1]: Distribution of patients in the three groups of asthma control.

FEV₁ and its correlation with ACT: The mean percentage predicted of FEV₁ was 52.01±14.47. The FEV₁ of three patients was more than 80% which was normal. 47% of the patients had FEV₁ between 30% to 50% and 45% patients had FEV₁ between 50% to 80% [Table/Fig-2]. The spearman's correlation between asthma control test and FEV₁ was 0.2758 with a p-value of 0.0414 which was statistically significant [Table/Fig-3]. Correlation of ACT with study parameters [Table/Fig-4].

FEV1	Number of patients
<30%	1
30-50%	26
50-80%	25
>80%	3

[Table/Fig-2]: Distribution of patients in FEV₁ groups.



[Table/Fig-3]: Scatter plot of correlation between ACT and FEV₁.

ACT: Y axis FEV₁: X axis

Parameter	Mean±SD	Correlation with ACT	p-value
FEV ₁	52.01±14.47	0.2758	0.0414
PEF _R	234.54±83.26	0.2575	0.05
AEC	456.34±266.9	-0.4583	<0.001
Serum magnesium	1.99±0.21	0.3414	0.010

[Table/Fig-4]: Summary of results.

Peak Expiratory Flow Rate (PEF_R) and its correlation with ACT:

The mean was PEF_R 234.54±83.26 [Table/Fig-5]. The correlation between asthma control test and PEF_R was 0.2575 with a p-value of 0.05 which was not statistically significant.

Absolute Eosinophil Count (AEC) and its correlation with ACT:

The mean AEC was 456.34 cells μL with a standard deviation of 266.9. A majority of patients had AEC between 251-500 cells μL,

PEFR	Number of patients(n=55)
<200 L/MIN	28
200-400 L/MIN	25
>400 L/MIN	2

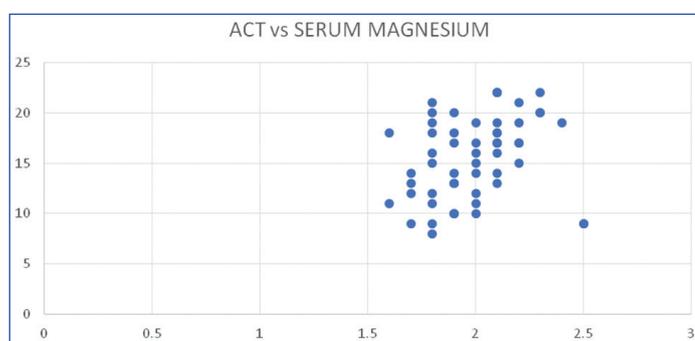
[Table/Fig-5]: Distribution of PEFR among patients.

47% (26 patients) [Table/Fig-6]. The spearman correlation between Asthma control test and AEC was -0.4583 with a p-value of <0.001, which was statistically significant.

AEC cells μ L	Number of patients (n=55)
100-250	12
251-500	26
501-750	8
>750	9

[Table/Fig-6]: Levels of peripheral eosinophils in the study population.

Correlation of ACT and levels of serum magnesium: The mean serum magnesium was 1.99 ± 0.21 . The spearman correlation of asthma control test with serum magnesium was 0.3414 with a p-value of 0.010, which was statistically significant [Table/Fig-7].



[Table/Fig-7]: Scatter plot of ACT and Serum magnesium levels.
ACT: Y axis Serum magnesium: X axis

DISCUSSION

Pulmonary function tests and asthma control test: In present study, Asthma control test and FEV1 had a positive correlation with a p-value of 0.0414 which is statistically significant.

Obianulu O et al., studied the correlation between ACT and prebronchodilator FEV1 in Nigerian with bronchial asthma. They included 46 asthmatics and found that ACT has a positive correlation with FEV1 similar to present result [11]. Papokosta D et al., studied the relationship of ACT with FEV1 and exhaled nitric oxide (FeNO) in 160 asthmatics. They found that ACT had a positive correlation with prebronchodilator predicted FEV1 % ($r=0.177$, $p=0.25$) and negative correlation with FeNO ($r=-0.211$, $p=0.007$). They concluded that ACT score was found to reflect lung function and inflammation in Greek asthmatic population [12].

Asthma control and PEFR: No studies were reported on asthma control and PEFR in adults. In present study, ACT and PEFR did not have a significant positive correlation (Spearman's correlation-0.2575, p-value 0.05). In a study performed by Chan M et al., comparing asthma control test and PEFR showed no correlation in paediatric population [13].

Asthma control test and serum magnesium levels: Daliparty VM et al., conducted a cross-sectional study on the effect of serum magnesium levels on asthma control in 160 patients. They concluded that serum magnesium levels are correlated positively with asthma symptom control. It can be inferred from this study that serum magnesium levels might be used as a biomarker in assessing control or severity of asthma [14].

Kilic H et al., did a case control study with 50 patients and 40 controls in which the relationship between serum magnesium values and lung function parameters were studied. It was found that lung functions

were significantly lower in patients with hypomagnesemia [8]. From these studies it can be inferred that serum magnesium levels are associated with asthma control.

In present study, asthma control test had a significant positive correlation with serum magnesium levels. None of the patients in present study had hypomagnesemia, the mean levels of serum magnesium was 1.99 mg/dL. It has to be noted at this point that serum magnesium levels are not true indicators of magnesium levels in body.

A magnesium concentration of less than 1.6 mg/dL suggests hypomagnesemia, however it does not lead to manifestation of symptoms and signs, until it is less than 1.2 mg/dL in the serum. Measurement of the serum magnesium level however might not imply accurately the levels of intracellular magnesium. Intracellular depletion of magnesium may be seen despite a normal serum concentration. Estimation of magnesium concentration within the cells is not usually done because of the difficulty in performing tissue and cellular assays [15].

Asthma control test and Absolute Eosinophil Count (AEC): Casciano J et al., conducted a study to determine whether healthcare resources use and expenditure vary by eosinophil levels among patients with asthma. They included 2164 patients and found that patients with elevated eosinophil levels had significantly greater mean annual hospital admissions. From this study it can be concluded that higher eosinophil count is associated with poor asthma control [16].

In present study, asthma control test had significant negative correlation with AEC. Spearman's correlation value was -0.4583 with a p-value less than 0.001. It is in line with the previous studies showing that increased blood eosinophils are associated with poorly controlled asthma [17].

Limitation(s)

Asthma being more prevalent condition among Indian population, a larger sample size would have been more representative.

CONCLUSION(S)

Asthma control test score had a significant positive correlation with FEV1 and serum magnesium levels. It also had significant negative correlation with AEC (inflammatory marker). Hence, Asthma control test can be used as tool for treatment response in the current COVID-19 pandemic situation and also in resource limited settings.

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