ORIGINAL ARTICLE

RELATIONSHIP BETWEEN ASTHMA CONTROL SCORE AND SMALL AIRWAY DYSFUNCTION IN PATIENTS WITH BRONCHIAL ASTHMA

Hussain Ahmad, Rukhsana Javed Farooqi, Saadia Ashraf

Department of Pulmonology, Khyber Teaching Hospital, Peshawar - Pakistan

ABSTRACT

Objective: To determine the correlation between asthma control score and small airway dysfunction.

Material and methods: Patients presenting to the OPD of Pulmonology with a diagnosis of asthma were enrolled in the study. Their asthma control was assessed via a validated scale rating from 5-25 (Asthma control test) and their spirometry was performed. Mid-expiratory flow (FEF25-75%) was taken to measure small airway dysfunction. All the spirometric parameters including FEV1, FVC, FEV1/FVC, PEFR, and FEF25-75% were obtained. The data was analyzed via SPSS 22. Pearson's correlation between ACT score and FEF25-75% was calculated. A p-value of <0.05 was taken as significant.

Results: A total of 78 adult patients were enrolled of which 42.3% were males. The Mean age of them was 46.79 (±17.7), BMI 26.86 (± 7.2), and FEV1 was 53.1% predicted (± 20.7). Five percent of patients had normal FEV/FVC but low FEF25-75%. The Pearson's correlation between ACT score and FEF25-75% was 0.289 (p=008). After linear regression analysis, an R2 of 0.11 was obtained.

Conclusion: We found a statistically significant but weak correlation between asthma control score and small airway dysfunction. FEF25-75% may be of value in the diagnosis of asthma when the patient has symptoms and conventional spirometry is normal.

Keywords: Asthma, Asthma Control Test, Small Airway Dysfunction

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INTRODUCTION

Asthma is a common respiratory disorder affecting all age groups. It is characterized by remissions and exacerbations of respiratory symptoms like cough, chest tightness, and difficulty breathing. It affects approximately 300 million people in the world resulting in high morbidity and mortality. The estimated prevalence ranges from 1-18% of the population among different countries. [1] The exact prevalence of asthma in Pakistan is not known but it is estimated to be 4.3%. [2]

The GINA guidelines recommend Spirometric indices like FEV1 and FEV1/FVC to diagnose the disease and monitor the response to treatment. It correlates well with the severity of the disease. [3] However normal values of these indices cannot exclude asthma mainly because alteration of FEV1 is observed only in overt airflow limitation. The reason behind this is that FEV1 represents mainly the obstruction in major airways while asthma affects small airways as well. Small airways are affected in about 65% of patients with asthma. [4] Small airway disease is related to more severe asthma. [5] FEF25%-75% as compared to FEV1 is more sensitive in detecting small airway dysfunction as theoretically, it is less effort dependent and it does not include airflow at high lung volumes as compared to FEV1. [6]

The utility of FEF25%-75% can be of value in detecting diseases of small airways that can be an important target for various inhaled medicines with ultrafine particles. Whether determination and interpretation of FEF25%-75% has any added value to FEV1 in asthma management is a matter of debate. A study conducted by Quanjer et al. (2014) reported only 3% of the study population with normal FEV1 and FVC had a decreased FEF25%-75% and concluded that the determination of FEF25-75% does not contribute to clinical decision-making. [7] On the other hand, a more recent study (retrospective) conducted by Qin et al. (2021) using a dataset of 1801 patients with confirmed asthma enrolling adult patients (18-65years) has shown FEF25%-75% as a better index of severity of asthma and airway hyperresponsiveness than FEV1. [8]

The rationale of our study was that the literature

Correspondence
Dr. Rukhsana Javed Farooqi
Assistant Professor
Department of Pulmonology, Khyber Teaching Hospital, Peshawar, Pakistan
Email: rukhsanafarooqi1995@gmail.com
Phone: +92-333-9125203
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about small airway dysfunction and its relationship with pulmonary functions is limited, focused mainly on FEV1 and the results are conflicting. This study was designed to determine the correlation between asthma control score and small airway dysfunction which may be helpful regarding treatment particularly targeting small airways to achieve better asthma control.

MATERIALS AND METHODS

This cross-sectional descriptive study was performed over patients presenting to the Outpatient Department of Pulmonology of Khyber Teaching Hospital with a diagnosis of asthma were enrolled in the study. Their asthma control was assessed via a validated scale rating from 5-25 (Asthma control test) and their spirometry was performed. Mid-expiratory flow (FEF25-75%) was taken to measure small airway dysfunction. [10] All the spirometric parameters including FEV1, FVC, FEV1/FVC, PEFR, and FEF25-75% were obtained. Patients with acute severe asthma, when spirometry could not be performed or contraindicated, and patients with associated pneumonia, angina, Pneumothorax, bronchiectasis, cardiac or respiratory failure were excluded. A Sample size of 78 was calculated via OpenEPI, keeping the confidence level of 97%, and a proportion of 4.3%. data was collected through convenient nonprobability sampling.

After approval from IREB of the hospital (No: 401/DME/KMC, dated: 11/7/2023), all patients fulfilling the inclusion criteria were assessed via ACT as part of the management protocol. A trained respiratory technician performed the spirometry to determine FEF25-75% and asthma control score. The latest model of computer-based spirometer (spirolab III) was used. A hospital MR number, gender, Age, weight, and height of the patients were noted. Spirometry readings of FEV1 and FEF25-75% were recorded in a proforma.

The data was analyzed via SPSS 22. Mean, and std deviation was calculated for age, FEV1, PEFR, FEF25-75%, and Asthma control score. Frequency and percentages were calculated for gender. Pearson correlation was applied to determine the correlations between FEV1, FEF25-75%, and Asthma control scores. A p-value of < 0.05 was taken as significant. Linear regression analysis was performed to determine the true relationship between these variables.

RESULTS

A total of 78 adult patients were enrolled, 42.3% of these were males. Mean age was 46.79 (± 17.7), BMI=26.86 ± 7.2, FEV1 53.1% predicted (± 20.7), mean FEV1/FVC 64 (± 9. 6). Five percent of patients had normal FEV/FVC but low FEF25-75%. The Pearson's correlation between FEF25-75% and ACT was 0.289 (p=008). After linear regression analysis, R2 of 0.11 was obtained (Figure: 01). There was a significant correlation between FEV1 (% predicted) and FEF25-75% with R2 0.74 (shown in Figure: 02)

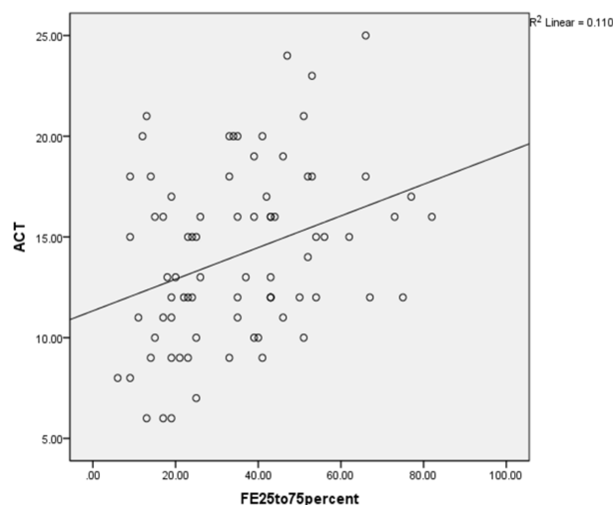

Fig 1: Correlation between FEF25-75% and Asthma Control Test score.

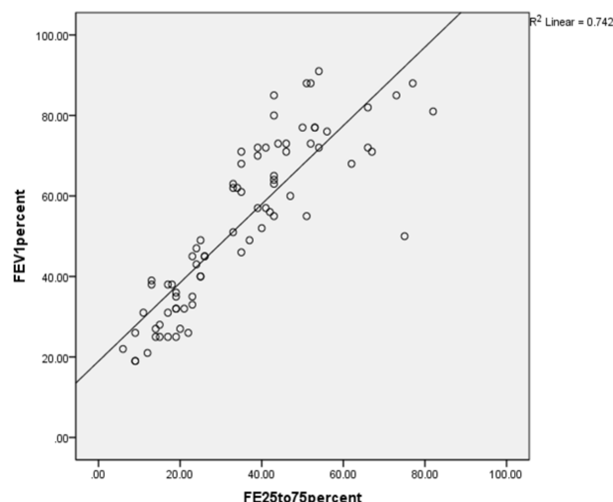

Fig 2: Correlation between FEV1% predicted and FEF25-75% predicted.

DISCUSSION

Chronic airway inflammation is one of the main characteristics of bronchial asthma. It involves both small and large airways. Small airways are rather affected earlier in the course of the disease. Small airway dysfunction can be seen even in patients with mild asthma who have normal traditional spirometric indices.[11] Although FEV1 is the established parameter for diagnosis and grading the severity of bronchial asthma, it can be normal in some patients particularly those with a milder form of the disease or cough variant asthma. Further investigations are

required in such patients to confirm the diagnosis. Studies suggest that asthmatic patients may have normal FEV1, FVC, and still an abnormally low FEF25-75% that is a measure of small airway dysfunction. [12] Small airway dysfunction (FEF25-75%) is related to asthma symptoms, its long-term persistence, and poor outcomes independent of large airway involvement.[13]

Our study found that FEF25-75% has a weak correlation with Asthma control test scores, which may indicate that both clinical parameters and pulmonary functions need to be assessed separately. FEF25-75% has been suggested as an additional tool for the assessment of asthma control.[14]

The second conclusion of our study was that FEF25-75% was low in 5% of our study population in whom conventional spirometric indices were normal. A study conducted by Quin et al has revealed that FEF_{25-75}% represents small airway function and it is more sensitive at reflecting bronchial hyperresponsiveness, and disease severity as compared to FEV_1% in asthmatic patients. The authors suggested further assessment of FEF25-75% in asthma management, particularly for those with small airway dysfunction who present with normal FEV_1%. [8] Hence, measuring FEF25-75% may be a more sensitive parameter in diagnosing bronchial asthma, particularly the milder form of the disease.

Lastly, FEF25-75% was found to be strongly correlated with FEV1. Similar results have been shown by a post-hoc analysis of a tiotropium-based trial showing a moderate to high correlation between FEV1 and FEF25-75% (r =0.73-0.80) and the later was shown to be a more sensitive measure of the treatment response. [15]

A retrospective analysis of spirometry data obtained from 22767 patients by Quanjer et al. concluded that Measurements of maximum mid-expiratory flow (FEF25–75%) and FEF75% are highly correlated with conventional spirometry indices, which are in contrast to our results. Moreover, this analysis suggested that these maneuvers (FEF25-75, FEF75%) provide little or no additional information over and above the traditional spirometry indices. The main logic behind their conclusion was that a decrease in FEF25-75% in those patients having normal FEV1 and FEV1/FVC can occur because of a reduction in volume rather than lung function impairment by itself. However, this study included small children of age as low as 3 years and analyzed retrospective spirometry data and not the real patient symptoms. [7]

The therapeutic significance of small airway dysfunction in asthma has been explored in another study, concluding that delivering inhaled corticosteroid medicines to distal airways via HFA-based formulation may have the potential to treat bronchial asthma more effectively with lower steroid dose as compared to CFC formulations. [16]

Small airways may be a potential target for the treatment of airway diseases including asthma. Further research is needed to confirm whether the assessment of small airway function has a clinical impact and is placed in routine clinical practice.

A single parameter (FEF25-75%) taken to measure small airway dysfunction limits the efficacy of this study. Further large-scale experimental studies are needed to strengthen the evidence in this regard.

CONCLUSION

The study concludes that there was a significant but weak correlation between asthma control score and small airway dysfunction but a strong correlation between FEV1 and FEF25-75% predicted ($R2=0.74$). Clinical variables (ACT) cannot reliably be predicted from spirometric variables (FEF25-75%) in these patients, hence both need to be assessed separately. Moreover, the FEF25-75% may be of value in diagnosing asthma when the patient has symptoms and conventional spirometry is normal.

REFERENCES

1. Levy ML, Bacharier LB, Bateman E, Boulet LP, Brightling C, Buhl R, et al. Key recommendations for primary care from the 2022 Global Initiative for Asthma (GINA) update. NPJ Prim Care Respir Med. 2023 Feb 8;33(1):7.
2. Khan MA. Monthly and seasonal prevalence of asthma and chronic obstructive pulmonary disease in the District Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan. The Egyptian Journal of Bronchology. 2022 Dec 3;16(1):63.
3. Aburuz S, McElnay J, Gamble J, Millership J, Heaney L. Relationship Between Lung Function and Asthma Symptoms in Patients with Difficult to Control Asthma. Journal of Asthma. 2005 Jan 2;42(10):859–64.
4. Usmani OS, Singh D, Spinola M, Bizzi A, Barnes PJ. The prevalence of small airways disease in adult asthma: A systematic literature review. Respir Med. 2016 Jul;116:19–27.
5. Carr TF, Altisheh R, Zitt M. Small airways disease and severe asthma. World Allergy Organization Journal. 2017;10:20.
6. Rao DR, Gaffin JM, Baxi SN, Sheehan WJ, Hoffman EB, Phipatanakul W. The Utility of Forced Expiratory Flow between 25% and 75% of Vital Capacity in Predicting Childhood Asthma Morbidity and Severity. Journal of Asthma. 2012 Aug 28;49(6):586–92.
7. Quanjer PH, Weiner DJ, Pretto JJ, Brazzale DJ, Boros PW. Measurement of FEF25-75% and FEF75% does not contribute to clinical decision making. European Respiratory Journal. 2014 Apr 1;43(4):1051–8.
8. Qin R, An J, Xie J, Huang R, Xie Y, He L, et al. FEF25-75% Is a More Sensitive Measure Reflecting Airway Dysfunction in Patients with Asthma: A Comparison

Study Using FEF25-75% and FEV1%. J Allergy Clin Immunol Pract. 2021 Oct;9(10):3649-3659.e6.

9. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test-A survey for assessing asthma control. Journal of Allergy and Clinical Immunology. 2004 Jan;113(1):59–65.

10. Pellegrino R. Interpretative strategies for lung function tests. European Respiratory Journal. 2005 Nov 1;26(5):948–68.

11. Carr TF, Altisheh R, Zitt M. Small airways disease and severe asthma. World Allergy Organization Journal. 2017 Dec;10:1-9.

12. Pisi R, Aiello M, Frizzelli A, Feci D, Aredano I, Manari G, Calzetta L, Pelà G, Chetta A. Detection of small airway dysfunction in asthmatic patients by spirometry and impulse oscillometry system. Respiration. 2023 Jul 26;102(7):487-94.

13. Siroux V, Boudier A, Dolgopoloff M, Chanoine S, Bousquet J, Gormand F, Just J, Le Moual N, Nadif R, Pison C, Varraso R. Forced midexpiratory flow between 25% and 75% of forced vital capacity is associated with long-term persistence of asthma and poor asthma outcomes. Journal of Allergy and Clinical Immunology. 2016 Jun 1;137(6):1709-16.

14. Dang P, The, Van TT, Duong-Quy S. Study of forced expiratory flow of 25% - 75% values (FEF25-75) in the control of asthma according to GINA. J Func Vent Pulm 2020;33(11):42-6..

15. Szefler SJ, Goldstein S, Vogelberg C, Bensch GW, Given J, Jugovic B, Engel M, Moroni-Zentgraf PM, Sigmund R, Hamelmann EH. Forced Expiratory Flow (FEF 25–75%) as a Clinical Endpoint in Children and Adolescents with Symptomatic Asthma Receiving Tiotropium: A Post Hoc Analysis. Pulmonary Therapy. 2020 Dec;6:151-8.

16. Martin RJ. Therapeutic significance of distal airway inflammation in asthma. Journal of Allergy and Clinical Immunology. 2002 Feb 1;109(2):S447-60.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Ahmad H	✓	×	✓	×	✓	×
Farooqi RJ	✓	✓	×	✓	✓	×
Ashraf S	×	✓	×	×	✓	×

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Ethical Review Board of Khyber Medical College, Peshawar. Vide No. 401/DME/KMC. Dated: 11 07 2023

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