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Original Article

Aspergillus Antibodies: Association with Severity of Disease in Patients Suffering from Asthma

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ABSTRACT

Objective: To determine the association of anti-aspergillus antibodies and other socio-demographic factors with severity of disease among patients suffering from asthma.

Study Design: Comparative cross-sectional study.

Place and Duration of Study: Pulmonology Department, Pak Emirates Military Hospital, Rawalpindi Pakistan, from Dec 2020 to May 2021.

Methodology: One hundred and fifty patients of asthma diagnosed for more than one year by a consultant respiratory physician were included in the study. Severity of asthma was assessed at the time of initial assessment and classed as mild, moderate or severe on the basis of symptoms and lung function tests. Baseline Laboratory investigations along with serum for anti-aspergillus antibodies were sent as well at the same time. Association of presence of aspergillus antibodies in serum along with their demographic factors was assessed with severity of illness in our study participants.

Results: Out of 150 patients of asthma, 65(43.3%) had mild illness, 44(29.3%) had moderate and 41(27.3%) had severe illness. Mean age of the study participants was 41.232±8.91 years. 115(76.7%) were positive for IgG anti-aspergillus antibodies while 35(23.3%). Presence of IgG anti-aspergillus antibodies had statistically significant relationship with sever asthmatic illness in our study population (p-value<0.001).

Conclusion: More than quarter of the study participants had severe form of asthmatic illness in this study and presence of IgG anti-aspergillus antibodies emerged as a factor strongly associated with severity of illness among patients of persistent asthma included in our study.

Keywords: Anti Aspergillus Antibodies, Asthma, IgG, Severity of Disease.

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INTRODUCTION

Asthma has been one of the most studied illnesses of the respiratory tract. This chronic condition is prevalent in all parts of the world including Pakistan.[1,2] Asthma not only affects the respiratory system but the hypoxic effects from this illness affects almost all the organ systems compromising the overall quality of life of the individual.[3] Severity of asthma is considered as an important predictor for short term response to treatment and long term prognosis of illness.[4] Clinicians and asthma associations have devised various methods to assess the severity of illness incorporating the clinical symptoms and lung function tests.[5] Approach of the treating physician and management plan differs to a great extent depending upon the severity of illness.[6] Multiple factors including age, gender, comorbid medical illnesses, comorbid bacterial or fungal infections and initial response to medications have been associated with severe form of illness among patients suffering from this obstructive airway disease.[6]

Literature of recent past has supported the association of asthma and fungal involvement among different populations of the world. Agarwal *et al.*, in 2011 concluded that there was convincing evidence for the presence of fungal involvement in patients suffering from asthma and a strong association was found between fungal sensitization and severity of asthma.[7] Kozlova *et al.*, published a prospective study in 2017 and revealed that incidence of ABPA was as high as 4% in the patients with asthma and 11% in those with severe asthma and fungal sensitization.[8] A systematic review and meta-analysis was published by Kwizera *et al.*, in 2019 to assess the burden of fungal asthma in Africa. They included studies from 13 African countries and revealed that fungal

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sensitization and infection was common among the patients suffering from asthma. They did not study the correlation of fungal involvement with severity of asthma or response to treatment.[9]

Fungal involvement can complicate the picture of asthma and can prolong or intensify the treatment of asthma. Zubairi *et al.,* published a study in 2014 from data generated from the biggest city of Pakistan, Karachi establishing the association of higher concentration of indoor Aspergillus spp. with asthma exacerbation in adult population. Limited local data is available regarding relationship of fungal sensitization and severity of asthmatic illness. We therefore planned this study with the rationale to determine the association of aspergillus antibodies and other socio-demographic factors with severity of disease among patients suffering from asthma.

METHODOLOGY

This comparative cross-sectional study study was conducted at pulmonology department of Pak Emirates Military Hospital Rawalpindi, Pakistan from December 2020 to May 2021. Sample size was calculated by WHO sample size calculator by using the population prevalence proportion of positive IgG aspergillus antibodies in patients of asthma as 10.8%.[11] Non-probability consecutive sampling was done from the patients of asthma reporting in the medical and pulmonology outpatient department of Pak-Emirates Military Hospital Rawalpindi.

Inclusion Criteria: All patients between the age of 18 and 60 years who had been suffering from asthma for at least one year and have given written informed consent were included in the study.

Exclusion Criteria: Patients with allergies secondary to identifiable causes and history of fungal infections before the diagnosis of asthma were not included in the study. Patients with any other chronic physical illness or those with immunocompromised status were also excluded from the study. Pregnant women or those with unclear diagnosis were also not include in the study. After the application of inclusion and exclusion criteria, 157 subjects were included in the final analysis.

The sample was drawn from the patients of asthma reporting in medical and pulmonology OPD of PEMH RWP and fulfilling the inclusion and exclusion criteria. After getting ethical approval from the hospital ethical review board committee (IREB letter no A/28/EC/304/2021) and written informed consent form all the participants of this study IgG anti-aspergillus antibodies were assessed in serum of all the participants. 5mL of blood was obtained, and centrifuged to collect the supernatant for the Aspergillus-specific IgG measurement. Enzyme-linked immunosorbent assay (ELISA) was the method used for this purpose. A fumigate IgG, IgM antibody quantitative detection kit was used in laboratory of Armed Forces Institute of Pathology for this purpose. The Aspergillus-specific IgG critical value that was lower than 50AU/mL was considered negative, whereas a value of higher than 60AU/mL was considered positive.[12]

The EPR-3 guideline classification was used to classify the asthmatic illness on the basis of severity. Mild, moderate and severe classes were made for persistent asthma incorporating duration of symptoms, night time awakenings, use of beta-2 agonist, lung functions and exacerbations requiring oral corticosteroids.[13]

Descriptive statistics were used to describe the characteristics of participants and the severity of illness. Variables in this study included age, gender, smoking status and anti-aspergillus antibodies positivity. All statistical analysis was performed using Statistics Package for Social Sciences version 24.0. Pearson chi-square analysis was done to find the relationship between variables and severity of illness with considering *p*-values equal to or less than 0.05 as significant.

RESULTS

A total of 150 patients of asthma were included in the study. Mean age of the study participants was 41.232±8.91 years. 87(58%) were male while 63(42%) were female. Table-I showed the basic demographic characteristics of the study population included in our analysis. On the basis of severity, 65(43.3%) had mild illness, 44(29.3%) had moderate and 41(27.3%) had severe illness. 115(76.7%) were positive for IgG anti-aspergillus antibodies while 35(23.3%). Table-II showed that on application of Pearson Chi-square test, presence of IgG anti-aspergillus antibodies had statistically significant relationship with sever asthmatic illness in our study population (*p*-value<0.001) while age (*p*-value-0.256), gender (*p*-value-0.570) and smoking status (*p*-value-0.669) of

individuals did not have any significant relationship with severity of illness.

DISCUSSION

Asthma is an obstructive airway disease, usually allergic response of body manifesting in multiple ways mainly causing problems related to respiratory system. Allergic response may be to any substance in the environment and may differ from person to person. Relationship of fungal sensitivity and exacerbation of acute attack of asthma with severe form of illness among the patients suffering from asthma has been studied in many parts of the world.[14] Various types of fungi exist in almost all the ecological systems across the globe which may be acting as antigens for a lot of patients suffering from allergic conditions. We therefore conducted this study with the objective to determine the association of anti-aspergillus antibodies and other socio-demographic factors with severity of disease among patients suffering from asthma.

Table-I: Characteristics of Study Participants

Study parameters	n(%)
Age (days)	
Mean+SD	41.232±8.91 years
Range (min-max)	18-60 years
Gender	
Male	87(58%)
Female	63(42%)
Severity of asthma	
Mild	65(43.3%)
Moderate	44(29.3%)
Severe	41(27.3%)
Tobacco smoking	
No	102(68%)
Yes	48(32%)
IgG anti-aspergillus antibodies	
Negative	115(76.7%)
Positive	35(23.3%)

Table-II: The Associated Factors Relating to Severity of Asthmatic Illness (The Chi-Square Analysis)

Factors	Mild	Moderate	Severe	*p*-value
Age				
18-40	44(67.7%)	32(72.7%)	23(56.1%)	0.256
>40	21(32.3%)	12(27.3%)	18(43.9%)	
Gender				
Male	40(61.5%)	26(59.1%)	21(51.2%)	0.570
Female	25(38.5%)	18(40.9%)	20(48.8%)	
IgG anti-aspergillus antibody				
Negative	58(89.2%)	39(88.6%)	18(43.9%)	<0.001
Positive	07(10.8%)	05(11.4%)	23(56.1%)	
Tobacco smoking				
Non Smoker	42(64.6%)	32(72.7%)	28(68.3%)	0.669
Smoker	23(35.4%)	12(27.3%)	13(31.7%)	

Denning *et al.*,[15] in 2006 published a summary of evidence regarding the link between fungi and severe asthma. They proposed the term "severe asthma with fungal sensitization" and demonstrated the close relationship of fungal involvement in severe form of asthmatic illness. They even went a step forward and discussed role of anti-fungal medications in such patients. Ours was a very basic study to look for association of fungal sensitization and severity of asthma and we found a statistically significant association between these two variables.

Khanbabaee *et al.*,[16] in 2012 published a similar study with objective to look for serum levels of IgG antibody for aspergillus and its relationship with severity of asthma among the children suffering from asthma. They established a significant relationship among the two and coined the idea to test the children presenting with acute asthma for these antibodies. Though, we targeted only adult population for our study but our results support he results generated by Khanbabaee *et al.*, among the pediatric population.

Ritesh Agarwal[17] in 2011 also recognized this phenomenon as new phenotype of asthma with a continuum of fungal sensitization, with asthma at one end and allergic bronchopulmonary aspergillosis at the other. He discussed only severe form of asthmatic illness in this regard and emphasized on more research for treatment options for this phenotype of asthma. We in our analysis included all the patients of persistent asthma may they be mild, moderate or severe and concluded that severe form of illness had more chances of having fungal sensitivity as compared to mild or moderate illness.

An interesting analysis was published in 2013 by Denning and Cole in journal of medical mycology regarding global burden of allergic broncho-pulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults.[18] They revealed that out of 193 million adults with active asthma worldwide, 4,837,000 patients (range 1,354,000-6,772,000) develop, allergic broncho-pulmonary aspergillosis. Though ours was an original study with small sample size but still our data set established a significant correlation between fungal sensitivity and severe asthmatic illness.

LIMITATION OF STUDY

Study subjects were recruited from one pulmonology unit of country therefore could not be considered representative of entire population of Pakistan. We used

Cross-sectional study design which cannot confirm the cause and effect relationship between the positive fungal sensitivity and severe asthmatic illness. Multiple confounding factors may be responsible for severe form of illness among the study participants which were not controlled at the baseline. Using our results as baseline, more studies could be done with better design across the country to establish this association.

CONCLUSION

More than quarter of the study participants had severe form of asthmatic illness in this study and presence of IgG anti-aspergillus antibodies emerged as a factor strongly associated with severity of illness among patients of persistent asthma included in our study.

Conflict of Interest: None.

Funding Source: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

ZAS & MZHM: Data acquisition, data analysis, critical review, approval of the final version to be published.

IZG & AMS: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RA & ZAS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

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.

REFERENCES

1. Caminati M, Vultaggio A, Matucci A, Senna G, Almerigogna F, Bagnasco D, et al. Asthma in a large COVID-19 cohort: Prevalence, features, and determinants of COVID-19 disease severity. Respir Med 2021; 176(#): 106261. https://doi.org/10.1016/j.rmed.2020.106261
2. Razzaq S, Nafees AA, Rabbani U, Irfan M, Naeem S, Khan MA et al. Epidemiology of asthma and associated factors in an urban Pakistani population: adult asthma study-Karachi. BMC Pulm Med 2018; 18(1): 184. https://doi.org/10.1186/s12890-018-0753-y
3. Hossny E, Caraballo L, Casale T, El-Gamal Y, Rosenwasser L. Severe asthma and quality of life. World Allergy Organ J 2017; 10(1): 28. https://doi.org/10.1186/s40413-017-0159-y4
4. Stubbs MA, Clark VL, McDonald VM. Living well with severe asthma. Breathe (Sheff) 2019; 15(2): e40-e49. https://doi.org/10.1183/20734735.0165-2019
5. Calciano L, Corsico AG, Pirina P, Trucco G, Jarvis D, Janson C et al. Assessment of asthma severity in adults with ever asthma: A continuous score. PLoS One 2017; 12(5): e0177538. https://doi.org/10.1371/journal.pone.0177538
6. Kang HR, Song HJ, Nam JH, Hong SH, Yang SY, Ju S, et al. Risk factors of asthma exacerbation based on asthma severity: a nationwide population-based observational study in South Korea. BMJ Open 2018; 8(3): e020825. https://doi.org/10.1136/bmjopen-2017-020825
7. Agarwal R, Gupta D. Severe asthma and fungi: current evidence. Med Mycol 2011; 3(Suppl 1): S150-157. https://doi.org/10.3109/13693786.2010.504752
8. Kozlova YI, Frolova EV, Filippova LV, Uchevatkina AE, Aak OV, Klimko NN. Allergic bronchopulmonary aspergillosis in patients with asthma: Results of a prospective study. Ter Arkh 2017; 89(8): 13-16. https://doi.org/10.17116/terarkh201789813-16
9. Kwizera R, Musaazi J, Meya DB, Worodria W, Bwanga F, Kajumbula H, et al. Burden of fungal asthma in Africa: A systematic review and meta-analysis. PLoS One 2019; 14(5): e0216568. https://doi.org/10.1371/journal.pone.0216568
10. Zubairi AB, Azam I, Awan S, Zafar A, Imam AA. Association of airborne Aspergillus with asthma exacerbation in Southern Pakistan. Asia Pac Allergy 2014; 4(2): 91-98. https://doi.org/10.5415/apallergy.2014.4.2.91
11. Maurya V, Gugnani HC, Sarma PU, Madan T, Shah A. Sensitization to Aspergillus antigens and occurrence of allergic bronchopulmonary aspergillosis in patients with asthma. Chest 2005; 127(4): 1252-1259. https://doi.org/10.1378/chest.127.4.1252
12. Pollart SM, Elward KS. Overview of changes to asthma guidelines: diagnosis and screening. Am Fam Physician 2009; 79(9): 761-767.
13. Guo Y, Bai Y, Yang C, Gu L. Evaluation of Aspergillus IgG, IgM antibody for diagnosing in chronic pulmonary aspergillosis: A prospective study from a single center in China. Medicine (Baltimore) 2019; 98(16): e15021. https://doi.org/10.1097/MD.0000000000015021
14. van Tilburg Bernardes E, Gutierrez MW, Arrieta MC. The Fungal Microbiome and Asthma. Front Cell Infect Microbiol 2020; 10(3): 583418. https://doi.org/10.3389/fcimb.2020.583418
15. Denning DW, O'Driscoll BR, Hogaboam CM, Bowyer P, Niven RM. The link between fungi and severe asthma: a summary of the evidence. Eur Respir J 2006; 27(3): 615-626. https://doi.org/10.1183/09031936.06.00074705
16. Khanbabaee G, Enayat J, Chavoshzadeh Z, Tabatabaei SA, Gorji FA, Rezaei N. Serum level of specific IgG antibody for aspergillus and its association with severity of asthma in asthmatic children. Acta Microbiol Immunol Hung 2012; 59(1): 43-50. https://doi.org/10.1556/AMicr.59.2012.1.5
17. Agarwal R. Severe asthma with fungal sensitization. Curr Allergy Asthma Rep 2011; 11(5): 403-413. https://doi.org/10.1007/s11882-011-0217-4
18. Denning DW, Pleuvry A, Cole DC. Global burden of allergic bronchopulmonary aspergillosis with asthma and its complication chronic pulmonary aspergillosis in adults. Med Mycol 2013; 51(4): 361-370. https://doi.org/10.3109/13693786.2012.738312