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Clinico-Microbiological Profile of Lower Respiratory Tract Infections with Special Reference to *Aspergillus Species*

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ABSTRACT

Lower respiratory tract infections (LRTI) accounts for approximately 10% of world wide burden of morbidity and mortality. Discrimination between fungal colonization and infection is not easy and antifungal treatment is initiated empirically which is associated with an increase in adverse events and costs together with inappropriate therapy and increased mortality as treatment is delayed. To evaluate clinical, immunological, microbiological and radiological features of Aspergillus infection in patients with LRTI. A cross-sectional study design including 100 Patients of age >15 years with LRTI in which Aspergillus infection was suspected like bronchial asthma ,ABPA, Aspergilloma, Immunocompromised host etc .were subjected to investigations like Chest X-Ray and CECT Thorax, Sputum for fungal hyphae, Serum and BAL Galactomannan assay , IgG specific for Aspergillus and data was analysed using trial version of SPSS 16. The study showed that Serum and BAL galactomannan assay was positive in 25% of patients with LRTI. Sputum Aspergillus, Serum Galactomanan assay and IgG specific for Aspergillus were positive in 55%, 77% and 100% of patients respectively with radiological shadows suggestive of aspergilloma. Serum AEC>1000/mm3 and Total S.Ig E>100 IU/ml in 28% of patient. IgG specific for Aspergillus >8 U/ml was positive in 22% of patients. We therefore, conclude that S.IgG specific for Aspergillus is the most sensitive tool for Aspergiloma followed by serum Galactomannan assay, sputum for Aspergillus. So in highly Aspergillus infection suspected patients of LRTI, sending IgG specific for Aspergillus would save time and help in initiating therapy on time thereby decreasing mortality.

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Key Words

Respiratory tract infections, a.spergillus, immunological, microbiological

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INTRODUCTION

Infections of the lower respiratory tract is one of the common and important causes of human disease from the points of view of morbidity, mortality and economic cost to society. The spectrum of diseases ranges from mild mucosal colonisation or infection, acute bronchitis or acute exacerbation of chronic bronchitis, chronic obstructive pulmonary disease, to an overwhelming parenchymal infection with patient presenting with severe community acquired pneumonia.

Fungal pulmonary involvement presents particular characteristics that complicate the patient's management. Presence of fungi may represent a true infection although frequently it only implies colonization of the respiratory tract, leading to a very different management and prognosis. Discrimination between colonization and infection is not easy and, frequently, antifungal treatment is initiated associated with an increase in adverse events and costs.

Aspergillosis refers to the spectrum of disease caused by Aspergillus species. The clinical manifestations of aspergillosis vary. The spectrum of pulmonary disease ranges from noninvasive disease, such as with colonization of the organism or the presence of a fungus ball (aspergilloma), or an allergic response responsible for the syndrome of allergic broncho pulmonary aspergillosis (ABPA), to semi-invasive or invasive infections such as chronic necrotizing pneumonia and invasive pulmonary aspergillosis.

The manifestations of aspergillosis dependent upon both the site and the severity of involvement and host immune status. Although infection with Aspergillus has been reported involving virtually all organ sites, the upper airways, lungs and surrounding structures are those most frequently involved. It is additionally important to recognize the spectrum of disease attributed to aspergillosis, ranging from invasive diseases such as invasive pulmonary aspergillosis, tracheobronchial aspergillosis, chronic necrotizing pulmonary aspergillosis and invasive sinonasal aspergillosis, to noninvasive diseases such as aspergillus fungus ball, chronic pulmonary aspergillosis, allergic broncho pulmonary aspergillosis (ABPA) and allergic fungal sinusitis.

It is likely that chronic and allergic forms of pulmonary aspergillosis are sufficiently common to be considered a public health issue on a global scale[1]. The most common form of aspergillosis is undoubtedly chronic pulmonary aspergillosis secondary to treated tuberculosis. It is therefore likely that most patients with pulmonary aspergillosis will be living in the resource---poor settings where tuberculosis is most common.

Hence this study was conducted to evaluate clinical, immunological, microbiological and radiological features of Aspergillus infection in patients with LRTI.

MATERIALS AND METHODS

The present study was conducted in the Department of TB and respiratory disease, Institute Of Medical Sciences, Banaras Hindu University, Varanasi in collaboration with Department of Microbiology during the period of July 2016-June 2018 was a descriptive cross sectional study.

Patients with lower respiratory tract infection in which Aspergillus infection suspected, Patient of bronchial asthma with uncontrolled symptoms and suspicious of diagnosis ABPA, Patient with the diagnosis of aspergilloma on radiological basis, Patients above the age group of 15 and above will be selected for the study and after due consent and detailed history regarding past tubercular infection. Other investigations like HIV and blood sugars will be done to rule out immunocompromised states. A Chest X-Ray and CECT Thorax were taken. Sputum will be collected and subjected for microscopic examination for fungal hyphae. Serum and BAL samples will be collected and subjected for Galactomannan assay.

Patients coming from eastern part of Uttar Pradesh, adjoining area of Bihar, Jhark and Madhya Pradesh and Chhattisgarh. Patients selected from those admitted in the Department of Tuberculosis and Respiratory Diseases Institute Of Medical Sciences, Banaras hindu University, Varanasi.

First of all the Institutional Ethics Committee was requested to approve the protocol. Once protocol was approved, then prior to enrollment in the study the patient was evaluated to determine eligibility and was explained about the study purpose, procedures and patients responsibilities as the potential participant. When it had been established that the patient was eligible, written informed consent was obtained. Thus enrolled 100 patients receiving the diagnosis of LRTI were subjected to thorough history taking and clinical examinations. Vital signs were recorded and baseline routine investigations were sent including Complete blood count, Liver function test, Serum Creatinine, Blood urea nitrogen, Serum electrolytes, Blood sugar, specific blood tests for Aspergillus like serum galactomannan assay, ECG, X-ray chest PA view(if needed lateral view also) and CECT Thorax. Bronchoscopy was performed and send BAL samples for galactomannan assay. Arterial blood gas analysis was performed that gave information regarding PaO2, P/F Index and various other parameters. For microbiological analysis, sputum culture was also sent.

Statistical Analysis: All data were analyzed by using a statistical software package called statistical program for social sciences version 16 (SPSS, CHICAGO, IL). All calculations were also done by this program. Differences with $p<0.05$ were considered as statistically significant.

RESULTS AND DISCUSSIONS

100 patients with lower respiratory tract infections in which suspecting fungal infection and 30 age and sex matched controls were selected for study. Patients presented with breathlessness and other clinical features like cough, expectoration, hemoptysis, chest pain, fever, allergic rhinitis etc.

In this study among 100 patients, 11 were below or equal to the age of 20 yrs and 17 patients are above 60 yrs of age. So most of the patients are of middle age. The youngest patient was 16 yrs old and the oldest was 75 yrs old.

Out of 100 patients 30 patients were found to Aspergillus positive in sputum.

Out of 9 patients in which radiological shadows suggestive of aspergilloma, sputum for Aspergillus was positive in 5 patients.

Out of 9 patients with radiological shadows of aspergilloma, bronchoscopy was done only in 5 patients because other 4 patients did not give consent for bronchoscopy. BAL fluid galactomannan was positive in 1 patient.

Out of 9 patients with radiological shadows of aspergilloma, serum Galactomannan assay was positive in 7 patients which is significant.

All 9 patients in which radiological shadow suggestive of aspergilloma was present give positive result for IgG specific for Aspergillus. Which suggests positive correlation between aspergilloma and IgG specific for Aspergillus.

Out of 30 sputum positive for Aspergillus, in 9 patients bronchoscopy was performed in which BAL fluid Galactomannan assay was positive in 3 patients.

Out of 30 patients with sputum positive for Aspergillus, 13 patients showed positive results for serum galactomannan assay which is significant.

Out of 30 sputum positive patients 13 patients have IgG specific for Aspergillus >8 U/ml and 17 patients have IgG specific for Aspergillus <8 U/ml.

In sputum negative patients 9 patients have IgG specific for Aspergillus >8 U/ml and 61 patients have IgG specific for Aspergillus <8 U/ml.

It shows that all serological tests for Aspergillus lacks diagnostic values if performs alone.

Serum galactomannan assay was positive in 3 patients in which CECT Thorax has central bronchiectasis and also positive in 18 patients in which central bronchiectasis was absent in CECT Thorax.

All 13 patients in which central bronchiectasis were present in CECT Thorax give positive result for IgG specific For Aspergillus. It suggest that in those LRTI patients in which ABPA were suspected and central bronchiectasis was present in CECT Thorax give positive result for IgG specific for Aspergillus. It make positive correlation between ABPA and IgG specific for Aspergillus.

Out of 87 patients in which central bronchiectasis was absent in CECT Thorax, 9 patients (10.3%) give positive result for IgG specific for Aspergillus.

Lower respiratory tract infections is the leading infectious cause of death in human. Among the vast diversity of respiratory pathogens, fungi account for only a small portion of community-acquired and nosocomial pneumonias. Fungi may colonize body sites without producing disease or they may be a true pathogen, generating a broad variety of clinical syndromes.

Aspergillomas are formed when the fungus grows in a clump in a lung cavity. The cavity is often created by a previous condition like tuberculosis, lung abscess, lung cancer, cystic fibrosis, sarcoidosis etc.

ABPA is the best recognized manifestation of aspergillus associated hypersensitivity to aspergillus antigen in patients with long standing atopic asthma. The true prevalence of ABPA in patients of bronchial asthma is still not known. This may be due to the lack of a uniform diagnostic criteria and standardized test. Earlier the disease was thought to be a rarity but it has now become evident that ABPA is an important cause of significant lung damage.

Present study was carried out in 100 patients of LRTI of which >15 years in which fungal infection was suspected. In this study among the 100 patients, 11were below or equal to age of 20 years and 17 patients above 60 years old (Table 1). So most of the patients are of middle age. The youngest patient was 16 years old and the oldest patient was 75 years old. In stable patient respiratory rate is just above normal as severity increases respiratory rate (tachypnoea) and pulse rate (tachycardia) also increases.

Clinical profile of these patients showed that cough and expecporation were predominant symptoms presented in all 100 patients (100%) $p<0.001$ followed by episodic breathlessness in 65 patients (65%) $p<0.001$, hemoptysis in 28 patients (28%) $p=0.001$, chest pain in 18 patients (18%) $p=0.012$

In most of the patients chest X-RAY shows heterogenous opacities, prominent broncho vascular marking and in few patient there is fixed opacities.

An aspergilloma can be seen on both plain film and CT as an intracavitory mass surrounded by a crescent of air. The term " air crescent" is however really seen in recovering invasive pulmonary aspergillosis.

In our study, air crescent sign was present in 9 patients (9%) in CXR and CT Thorax. $p=0.089$.

CECT-thorax of 13% patients shows central bronchiectasis.

In our study total 40 patients diagnosed of bronchial asthma (confirmed with post bronchodilator reversibility of >200 ml and 12% improvement in FEV1 on pulmonary function tests).

Table 1 : Descriptive statistics of sputum for fungal hyphae esp. Aspergillus

Sputum For Aspergillus	case (n=100)		control (n=30)	
	No.	%	No.	%
Yes	30	30.0	0	0.0
No	70	70.0	30	100.0
Total	100	100.0	30	100.0

χ2=15.516, p=0.000

Table 2: CXR PA view and CT Thorax Vs sputum for Aspergillus

Sputum for fungal hyphae (aspergillus)	Fungal ball in CXR and CECT Thorax			
	Present		Absent	
	No.	%	No.	%
Yes	5	55.6	25	27.5
No	4	44.4	66	72.5
Total	9	100.0	91	100.0

χ2=3.076, p=0.079

Table 3: CXR PA view and CT Thorax vs BAL fluid Galactomannan assay

Bal fluid for Galactomannan Assay	Fungal ball in CXR and CECT Thorax			
	Present		Absent	
	No.	%	No.	%
Not done	4	44.4	76	83.5
Positive	1	11.1	5	5.5
Negative	4	44.4	10	11.0
Total	9	100.0	91	100.0

χ2=8.541, p=0.014

Table 4: CXR PA view and CT Thorax vs serum Galactomannan assay

Serum Galactomannan Assay	Fungal ball in CXR and CECT Thorax			
	Present		Absent	
	No.	%	No.	%
Positive	7	77.8	14	15.4
Negative	2	22.2	77	84.6
Total	9	100.0	91	100.0

χ2=19.218, p=0.000

Table 5: CXR PA view and CT Thorax Vs IgG sp for Aspergillus

IgG specific For Aspergillus	Fungal ball in CXR and CECT Thorax			
	Present		Present	
	No.	%	No.	%
>8 U/ml	9	100.0	13	14.3
<8 U/ml	0	0.0	78	85.7
Total	9	100.0	91	100.0

χ2=35.065, p=0.000

Table 6: sputum for Aspergillus vs BAL fluid Galactomannan assay

Bal fluid for Galactomannan Assay	Sputum for Aspergillus			
	Positive		Negative	
	No.	%	No.	%
Not done	21	70.0	59	84.3
Positive	3	10.0	3	4.3
Negative	6	20.0	8	11.4
Total	30	100.0	70	100.0

χ2=0.778, p=0.678

Table 7: Sputum for Aspergillus Vs Serum Galactomannan assay

Serum Galactomanan Assay	Sputum for Aspergillus			
	Positive		Negative	
	No.	%	No.	%
Positive	13	43.3	8	11.4
Negative	17	56.7	62	88.6
Total	30	100.0	70	100.0

χ2=12.885, p=0.000

Table 8: Sputum for Aspergillus Vs IgG specific for Aspergillus

IgG specific For Aspergillus	Sputum for Aspergillus			
	Positive	Negative		
	No.	%	No.	%
>8 U/ml	13	43.3	9	12.8
<8 U/ml	17	56.7	61	87.1
Total	30	100.0	70	100.0

χ2=5.905, p=0.015

Serum galactomannan assay was positive in 25 patients. BAL fluid Galactomannan assay was positive in 5 patient out of 20 patients in which bronchoscopy was performed.

Sputum for aspergillus was positive in 37 patients (37%) p<0.001 And positive in all 18 patients diagnosed of ABPA, which is similar to the study of Prasad *et al* 2007.

In our study BAL fluid galactomannan assay was positive in 3 patients out of 10 patients of bronchial asthma suspecting of ABPA. Literature for study of BAL for galactomannan assay in ABPA is not traceable. It is found that BAL fluid galactomannan assay is not diagnosed for ABPA.

In our study Air crescent sign was present in CXR and CT thorax of 9 patients. Our of 9 patients with aspergilloma sputum for aspergillus were positive in 6 patients. In 5 patients of aspergilloma bronchoscopy was performed. BAL fluid for galactomannan assay was positive in only 1 patient out of 5 patients. So BAL fluid for galactomannan assay is not very reliable in case of aspergilloma.

But serum galactomannan assay was positive in 6 patients of aspergilloma out of 9 patients (66.6%). This suggests that serum galactomannan assay is more sensitive than BAL fluid for galactomannan assay in case of aspergilloma.

IgG specific for aspergillus is positive (>8U/ml) in all 9 patients of aspergilloma (p<0.001).

18 patients diagnosed of ABPA present with abnormal radiograph had predominantly unilateral, upper zone abnormality with fleeting pulmonary infiltrates as the most common finding in 10 patients (66.6%). In previous studies fleeting shadows were found in 74% chakrabarti[2] and 40%[3]. Thus radiographic shadows neither establish nor exclude the diagnosis of ABPA. Radiographic infiltrates in patients of ABPA lay in correspondence with bronchial dilation, usually involving the upper lobes (VENDERSON 1968) and are mainly fleeting in character, which is evidence in our study also.

On CECT thorax examination, 9 patients had air crescent sign and central bronchiectasis were present in 13 patients (72.2%) which varied from 69%-76% in previous Indian studis (71% in Behera[4], 69% in Chakrabarti *et al* 2002 and 76% in Agarwal *et al* 2007). Previous studies reported that almost half of ABPA patients were misdiagnosed and treated with pulmonary TB Rajkumar[5], 16 out of 18 patients were prescribed antitubercular drugs sometimes in the course of their illness, which reflects the lower level of awareness among general physicians for ABPA.

Elevated total serum IgE or IgG specific for aspergillus are strong indicators of ABPA.

But in our study 28 patients with raised total IgE, only 18 were found to have ABPA, which highlights the fact that, like chest radiograph and CECT thorax, these serologic tests also lack reliability for diagnosis of ABPA if performed alone.

Any patient of long standing asthma, with high levels of peripheral blood AEC fleeting pulmonary infiltrates on social chest radiographs and persistently corticosteroids requirements for control of asthma, should always be investigated for ABPA.

CONCLUSION

We therefore, conclude that S.IgG specific for Aspergillus is the most sensitive tool for Aspergiloma followed by serum Galactomannan assay, sputum for Aspergillus. So in highly Aspergillus infection suspected patients of LRTI, sending IgG specific for Aspergillus would save time and help in initiating therapy on time thereby decreasing mortality.

REFERENCES

1. Agarwal, R., A.N. Aggarwal, D. Gupta, S.K. Jindal, 2009. 1. Aspergillus hypersensitivity and allergic bronchopulmonary aspergillosis in patients with bronchial asthma: Systematic review and meta-analysis. Int. J. Tuberc. Lung Dis., 13: 936-944.
2. Chakrabarti, A., S. Sethi, D.S.V. Raman and D. Behera, 2002. Eight-year study of allergic bronchopulmonary aspergillosis in an Indian teaching hospital. Mycoses, 45: 295-299.
3. Agarwal, R., D. Gupta, A.N. Aggarwal, A.K. Saxena and A. Chakrabarti,et al., 2007. Jindal SK. Clinical significance of hyperattenuating mucoid impaction in allergic bronchopulmonary aspergillosis: an analysis of 155 patients. Chest., 132: 1183-1190.
4. Behera, D., R. Guleria, S.K. Jindal, A. Chakrabarti and D. Panigrahi, 1994. 1. Allergic bronchopulmonary aspergillosis: a retrospective study of 35 cases. Indian J Chest Dis Allied Sci., 36: 173-179.
5. Kumar, R., 2000. 1. Allergic bronchopulmonary aspergillosis with aspergilloma mimicking pulmonary tuberculosis. Indian J. tub., 47: 103-105.