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# Fungal pneumonia in diabetes mellitus: a hospital based observational study

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## Abstract

**Introduction:** Pneumonia is caused by infection with bacteria, virus, fungi, and parasites. Lung infections by fungi are very less common as compared to that of bacteria. They mainly affect people with immune deficiency state like diabetes, taking corticosteroids, malignancy, hematological disease, HIV and post organ transplant patient receiving immunosuppressive therapy. Diabetes with poor glycemic control with pneumonia increases the risk of hospitalization. Fungal pneumonia is difficult to diagnose and is often made on a presumptive basis. It relies on a combination of clinical, radiologic, and microbiological factors.

**Aims And Objectives:** To find out the proportion of respiratory fungal infection in patient with diabetes mellitus presenting with pneumonia with clinical features and to find out culture and sensitivity pattern of different species of fungi causing pneumonia.

**Methods and Materials:** This hospital based observational study was done in a tertiary care centre for duration of 1 year. Inclusion criteria was all diagnosed cases of Diabetes Mellitus(fulfilling ADA criteria 2018) presenting with clinical picture suggestive of pneumonia and exclusion criteria were with patients < 12 years age, immunocompromized patient like HIV, organ transplant, any malignancy, COPD, CKD, on steroid and not giving consent. Ethical clearance was obtained .104 cases were taken up for study. Detailed history and physical findings with relevant pathological, biochemical, radiological investigations were performed and noted. Sputum for fungal and bacterial culture and sensitivity were done in all cases. Statistical analysis was done accordingly.

**Results:** Mean age of fungal pneumonia was 66.20 ± 8.56 years with male (60%) and female (40%) with male to female ratio 1.5:1. Clinical presentations of

fungal pneumonia were hemoptysis (40%), weight loss (80 %), chest pain (60 %), and breathing difficulty (60 %).Mean duration of diabetes was 13.5 ± 9.70 years with Mean ± SD FBS (243.65 ± 48.72), Mean ± SD PPBS (398.16 ± 57.67), Mean ± SD HbA1C (11.43% ± 2.78%).40% had HbA1c level in 9-10 % range and 60% were in > 10 %.Risk factors were smoking (40% ) and alcoholic (40%) . Causative organisms of fungal pneumonia were Candida(20%) and Aspergillus (80 %).Candida species isolated were Candida albicans 62.16%, Candida glabrata 5.40%, Candida krusei 2.70%, Candida tropicalis 5.40% and other Candida species 13.51% .Aspergillus species were Aspergillus flavus and Aspergillus fumigates .Candida albicans were resistance to fluconazole 30.43%, itraconazole 4.34 %, and amphotericin B 4.34 % of cases whereas Candida glabrata resistance to fluconazole 100%, itraconazole in 0%, voriconazole 0% and amphotericin B 0% was observed. Candida tropicalis resistance was seen to fluconazole 100%, itraconazole 0%, voriconazole 100% and amphotericin B 100% whereas Aspergillus resistance to fluconazole was 25%. Candida (100 %) had cavitary lesion with consolidation ,nodular opacity and air bronchogram whereas Aspergillus had nodular opacity (100%), consolidation (50%), air bronchogram (25%), cavity (50%), halo sign (25%) and air crescent sign (25%) on HRCT thorax.

**Conclusion**

Fungal pneumonia is common in diabetes patient with poor glycemic control. Our study showed pattern of respiratory fungal infection and prevalence of fungal pneumonia in diabetics in this north-east part of our country.

**Keywords:** culture sensitivity, diabetes mellitus, fungal pneumonia, pneumonia.

## Introduction

Pneumonia has been known as a disease entity since remote times, with definition of the condition traceable in ancient Greek, Roman, and Arabic writings[1] .It is characterized by inflammation of lung tissues with white blood cells infiltration in alveoli and often bronchioles accompanied by fibrinous exudate.Clinically, patients present with fever and chills, cough difficulty in respiration, chest pain as well as reduced lung expansion. Pathogens responsible for pneumonia can be diverse including bacteria, viruses and fungi to parasites. Severity of pneumonia can vary from mild needing only out-patient basis treatment to very serious condition requiring hospitalization even intensive care.

Although respiratory pathogens are vast in numbers, only small portion of nosocomial and community-acquired pneumonia are caused by fungi. Out of more than 1 lakh species only few fungi cause human infection and the most vulnerable organs are skin and lungs [2]. It includes aggressive human pathogen like Histoplasma or Blastomyces group or opportunistic invaders like Aspergillus and Candida species [3]. The involvement of lung can be broadly classified according to (a) allergic manifestation (b) actual infection [3–5].Endemic fungal pneumonias, such as histoplasmosis, may be predisposed by exposure to bat, rodent and bird droppings or other animal excreta .Risk of acquiring sporotrichosis is higher in gardeners and farmers because chances of cuts or puncture wounds are more during working with soil. As immunocompromized patients population are expanding globally which is generating more concerns of fungal respiratory infection. Colonization of fungi in different body sites may not produce any disease or they may be the true pathogen. Fungal lung infections are very worrisome because of difficulty in diagnosis and treatment. Fungi mainly affect people with immune

deficiency state like malignancy, diabetes, taking corticosteroids, HIV, hematological disease, post organ transplant patient receiving immunosuppressive therapy and people in certain geographic areas. Due to increase in immunocompromized states over recent years, dramatically increased incidence of fungal lung infections have been observed. Not only the incidence of fungal lung infection is on the rise there has been a substantial advance both in the diagnosis and treatment of fungal pneumonia [6].

Diabetes mellitus is a common chronic metabolic disorder with varied etiological factors characterized by reduced insulin secretion, decreased glucose utilization and increased glucose production sharing the common phenotype of hyperglycemia. Several distinct type of diabetes is caused by a complex interaction of genetic and environmental factors [3] .The prevalence of diabetes has dramatically risen in the last two decades with parallel increase in complications arising out of it. Fungal lung infection causes a serious threat to the management of diabetes complicated by poor glycolic control and other associated co morbidity owing to its difficulty in diagnosis and treatment.

Poor long-term glycolic control among patients with diabetes clearly increases the risk of hospitalization with pneumonia [7]. In diabetes several aspects of immunity such as polymorphonuclear leukocyte function i.e. leukocyte adherence, chemotaxis, phagocytosis and bacterial activity of serum are depressed. For patients with pneumonia, diabetes mellitus is also one of the most common underlying diseases[8].Fungal pneumonia is very difficult to prove and is often made on a presumptive basis. It relies on a combination of clinical, radiologic, and microbiological factors. Some fungi such as Candida albicans and some ubiquitous filamentous fungi (Aspergillus and Scedosporium) can be isolated from oropharyngeal and respiratory tracts as colonizers without any evidence of invasion or symptoms until a breakdown of tissue barrier or hosts immune system occurs.

Clinicians often overlook fungal pneumonia which may lead to inadequate treatment with increase in morbidity as well as mortality. Prolonged duration of symptoms with no antibiotic response should raise the suspicion of fungal pneumonia and be investigated accordingly.

This study was taken up in order to get some better understanding of the clinical pictures of fungal pneumonia and also its prevalence in diabetic individual in this part of the country.

**Aims and Objectives**

This study was carried out with the following aims and objectives.

1. To find out the proportion of respiratory fungal infection in patient with diabetes mellitus presenting with pneumonia.
2. To study the clinical features of fungal pneumonia.
3. To find out culture and sensitivity pattern of different species of fungi causing pneumonia.

**Materials And Methods**

This hospital based observational study was done in Assam Medical College and Hospital, Dibrugarh for duration of 1 year (between the 1st July 2018 to 30th June 2019).

**Study Population:** Patients who were diagnosed cases of Diabetes Mellitus, with clinical feature suggestive of pneumonia, admitted in Department of Medicine in Assam Medical College & Hospital, Dibrugarh.

**Inclusion Criteria**

All diagnosed cases of Diabetes Mellitus presenting with clinical picture suggestive of pneumonia,

**Exclusion Criteria**

Patients <12years age, immunocompromized patient like HIV, organ transplant, malignancy, COPD, CKD, patient on steroid and patients who refuse to give informed consent.

**Ethical Clearance**

Ethical clearance was obtained from Institutional Ethics Committee (H) prior to the onset of study. Informed written consent was taken from the patients.

**Method of Patient Selection**

A total of 124 patients were screened during the one year study period. Out of the 124 patients, 104 were taken up for the study after considering inclusion-exclusion criteria. Sputum culture for fungal and bacterial growth was done in all the selected 104 patients.

The history and physical findings were recorded as per a pre-designed proforma. A detailed general and systemic examination was done in all the patients. Important relevant pathological, biochemical, radiological (chest X-ray, CT scan thorax) investigations etc. were performed and noted. Sputum for fungal and bacterial culture and sensitivity were done in all cases.

**Case Definitions**

**A) Diagnosis of Diabetes**

Diabetes was defined according to the guidelines of Classification and Diagnosis of diabetes (American Diabetes Association, 2018)[9] which includes the following.

Table A: Ada,2018 Criteria For Diagnosis Of Diabetes[9]:

| |
|---|
| FPG 126 mg/dl (7.0mmol/L). Fasting is defined as no caloric intake for at least 8 h.* |
| OR |
| 2-h PG 200 mg/dl (11.1mmol/L) during OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.* |
| OR |
| HbA1C≥ 6.5% (48 mmol/mol). The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* |
| OR |
| In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose 200 mg/dL (11.1 mmol/L). |
| *In the absence of unequivocal hyperglycemia, results should be confirmed by repeat testing. |

**B) Diagnosis of Pneumonia**

Diagnostic criteria for CAP on clinical basis (BTS guidelines) (2009)[10]:

1. Symptoms of an acute lower respiratory tract illness (cough plus another lower tract symptom, e.g. dyspnea, pleuritic pain).

2. New focal chest signs on examination (e.g. bronchial breathing).

3. One of: sweating; fever; shivers; myalgia; or pyrexia > 30ºC.

4. No other explanation for the illness

**C) Diagnosis Of Fungal Pneumonia:**

**Fungal Infections Cooperative Group And The National Institute Of Allergy And Infectious**

**Diseases Mycoses Study Group (EORTC/MSG) Criteria For IPA[11]**

**PROVEN IPA (Invassive Pulmonary Aspergillosis)**

Specimen obtained by sterile technique like needle aspiration or biopsy in which hyphae are seen accompanied by evidence of tissue damage or culture for Aspergillus becomes positive

**Probable IPA**

1) Host factors

• Recent history of neutropenia (<500 neutrophils/mm for >10 days)

• Receipt of an allogeneic stem cell transplant

• Prolonged use of corticosteroids at a dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks

• Treatment with other recognized T-cell immunosuppressant, such as TNF-α blockers, specific monoclonal antibodies etc., during the past 90 days

• Inherited severe immunodeficiency (such as chronic granulomatous disease or severe combined immunodeficiency)

2) Clinical criteria

• Lower respiratory tract fungal disease

• The presence of 1 of the following 3 signs on CT

• Dense, well circumscribed lesions(s) with or without a halo sign

• Air crescent sign

• Cavity

3) Mycological criteria (any one) :

Mold in sputum, BAL fluid, bronchial brush, indicated by 1 of the following

• Presence of fungal elements indicating a mold

• Recovery by culture of Aspergillus or

• Indirect tests (detection of antigen or cell wall constituents)

• Galactomannan antigen detected in serum or BAL fluid

• β-D-glucan detected in serum

**Investigations Methodology**

**1. Sputum**

**Method of Sputum Collection:** 5-10 ml of three sputum samples were collected from patients in wide mouthed sterile container. Patients were asked to have deep cough to have proper sputum and preferably in morning. Sputum collection was done after mouth rinse and brush. Patients were instructed not to touch inside the collection container or lid.[12,13]

**Transport:** Sputum samples were transported directly after collection to the laboratory and processed immediately within 2 hours.

**Processing:** Concentration of sputum were done by adding 0.5gm of NALC (N-acetyl L-cysteine) in 100 ml of freshly prepared sodium citrate buffer and vortexed for 10-30 minute.[12,13]

**Direct Microscopy:** Sputum and colony growth were examined by direct microscopy after Gram staining, Ziel-Neelsen staining and KOH mounting.[12,14] Sputum specimens containing ≥10 leukocytes with mucus, but <25 squamous epithelial cells per low-power field (LPF, ×100), are unlikely to be contaminated by oropharyngeal flora.

**Culture:** Fungal Culture were done on Sabouraud dextrose agar containing Chloramphenicol (0.05mg/ml) and cyclohex[15], and bacterial culture were done on blood agar and MacConkey agar. The significant fungal and bacterial isolates recovered on culture were identified to the species level, using standard mycological and bacteriological procedures. For Candida sp. isolation, the tests performed include germ tube test, Dalmau culture plate, sugar assimilation and fermentation tests, and CHROM agar. Antibiotic sensitivity were done with disk diffusion method.[16,17] The fungal and bacterial growth were considered significant after repeated culture yielded same growth[18].

**2. FBS, PPBS**

Method: GOD/POD method

Principle: glucose is oxidized to glucoronic acid and hydrogen peroxide. Hydrogen peroxide further reacts with phenol and 4-aminopantipyrine by the catalytic action of peroxidase to form a red coloured quinoneimine dye complex. Intensity of coloured complex is directly proportional to the amount of glucose present.

Sample Material: serum, plasma. Glucose is reported to be stable in the sample for 7 days when stored at 2-8 ℃.

**3. HbA1c**

Glycosylated hemoglobin (GHb) has been defined operationally as the fastest fraction of hemoglobin – HbA1 (HbA1a, HbA1b, HbA1c) which elute first during column chromatography. The non-glycosylated hemoglobin, which consists of the bulk of the hemoglobin has been designated as HbA0.

A hemolysed preparation of the whole blood is mixed continuously for 5 minutes with a weakly binding cation-exchange resin. The labile fraction is eliminated during the hemosylate preparation and during binding. During the mixing HbA0 binds to the ion-exchange resin leaving GHb free in the supernant. After mixing period a filter is used to remove the resin from the supernant. The percentage is then calculated by finding out the GHb fraction and the total hemoglobin fraction. The ratio of the absorbance of GHb and the total hemoglobin of the control and test is used to calculate the percent of GHb of the sample.

**Sample Material:** whole blood preferably, fresh and collected in EDTA vial. GHb is reported to be stable foe 1 week at 2- 8 ℃.

**4. Chest X Ray**

Chest x ray was done by Siemens 800 mA Machine (Department of Radiology, Assam Medical College and Hospital. Chest x ray was analyzed noted for the presence or absence of cavity, number and location of cavities, infiltrates or air space opacities, consolidation, hilar enlargement fibrosis, pleural effusion and for any other findings suggestive of fungal pneumonia.

**5. HRCT Thorax**

HRCT thorax was done using Siemens somatom spirit dual slice CT (Department of Radiology, Assam Medical College and Hospital. It uses thinly colliminated slice of 1 - 1.5-2mm and increasing the KVp (130) and mA (260) different segments of the lung can be scanned. The width used 1000-2000 HU and level centre: 500-750 HU. CT images were studied for the presence of consolidation, air bronchogram, tree in bud appearance, air crescent sign, halo sign, pleural effusion, cavitary lesion, nodular opacity and any other finding suggestive of fungal pneumonia.

**Statistical Analysis:** Data collected were tabulated in Microsoft Excel Worksheet and computer based analysis was done using SPSS 20.0 software and Microsoft Excel 2010. Results were shown in terms of percentage and mean ± SD.

**Method of Data Collection:** Data were recorded in a predesigned proforma. Data included a detailed history, general and systemic examination and required investigations.

**Results and Observations**

104 patients of diabetes mellitus with pneumonia were studied and following figures and tables illustrate the important features and results of the study.

From the Fig .1 it is observed that majority of the pneumonia cases (30.70%) were in the age group of 61-70 years, followed by 23.07% in the age group of 51-60 years. In age group >12- 20, 21-30, 31-40, 41-50, 51-60, and >70 years the numbers of cases were 1 (0.96%),

2 (1.90%), 9 (8.65%), 15 (14.42%), 24 (23.07%), and 21 (20.19%) respectively. Mean age was 57.01 ± 15.56 years.

Out of 5 cases of fungal pneumonia,4 cases occurred above 60 years of age, and one case was seen in 41-50 years bracket.Mean age of fungal pneumonia was 66.20±8.56 years.

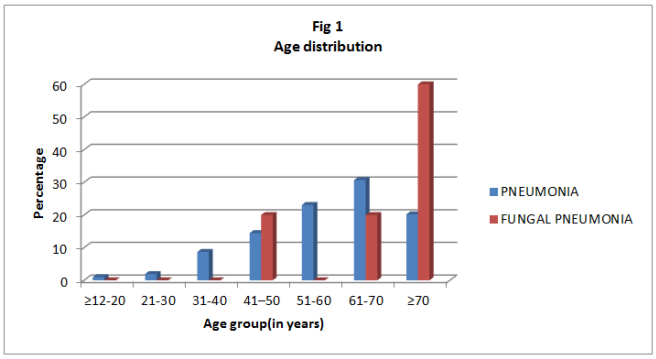


**Fig .1: Age Distribution of The Study Population**

From the Fig.2, majority (61.54%) of the pneumonia cases were male. The male to female ratio was 1.65:1.Out of the 5 cases of fungal pneumonia 3(60%) were male and 2 (40%) were female with male to female ratio 1.5:1.

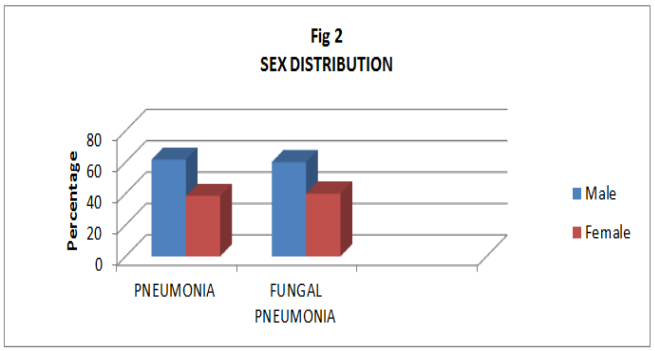


Table 1: Duration of Symptoms

| DURATION (in days) | PNEUMONIA | | FUNGAL PNEUMONIA(N=05) | |
|---|---|---|---|---|
| | Total Number (n=104) | Percentage (%) | Total Number (n=5) | Percentage |
| <7 | 79 | 75.96 | 0 | 0 |
| 7–21 | 20 | 19.23 | 2 | 40.00 |
| >21 | 5 | 4.81 | 3 | 60.00 |
| TOTAL | 104 | 100.00 | 5 | 100.00 |
| Mean ± S.D. | 5.39 ± 5.05 days | | 21.59 ± 9.73 days | |

Fig.2: Sex Distribution of the Study Population

As shown in Fig 3. Pneumonia patients presented with fever (100%),cough (77.89%),chest pain (39.42%), breathing difficulty (70.19%) whereas 10.57% had hemoptysis and 4.81% patients had weight loss. Fungal pneumonia presented with hemoptysis in 40% and weight loss in 80.00%, chest pain in 60.00% and breathing difficulty in 60.00% cases.

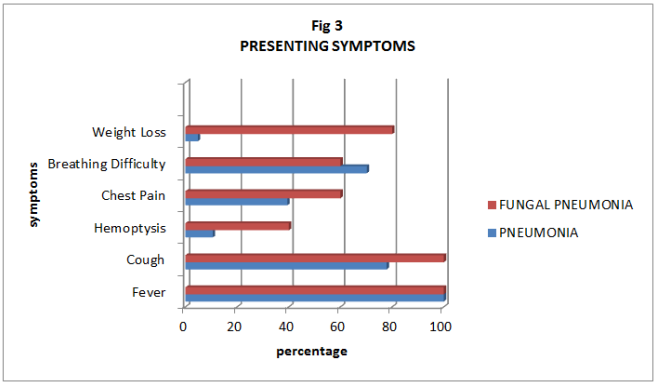


Fig.3 Presenting Symptoms of Fungal Pneumonia In Diabetes

From the above table 1. it is found that in pneumonia the most (75.96%) of the patients presented with illness duration of less than 7 days. 20 patients (19.23%) had illness duration from 1 week to 3 weeks and 5 patients had illness duration for more than 3 weeks. Mean ± SD of symptom duration was 5.39 ± 5.05days.Whereas 2 (40.00%) cases of fungal pneumonia had presented with symptoms duration 7-21 days, 3 (60.00%) cases more than 21 days. Mean duration of presentation for fungal pneumonia was 21.59 ± 9.73days.

Table 2: Duration of Diabetes Mellitus

| DURATION *(in years)* | PNEUMONIA | | FUNGAL PNEUMONIA | |
|---|---|---|---|---|
| | Total Number *(n=104)* | Percentage *(%)* | Total Number *(n=5)* | Percentage (%) |
| <5 | 29 | 27.88 | 0 | 0 |
| 5–10 | 52 | 50.00 | 1 | 20.00 |
| >10 | 23 | 22.12 | 4 | 80.00 |
| *Mean ± S.D.* | 8.52 ± 2.8 | | 13.5 ± 9.7 | |

As shown in table 2. most (50%) of the pneumonia patients had diabetes for 5-10 years duration. 27.88% patient had diabetes for less than 5 years and 22.12% patient had diabetes for more than 10 years duration. Mean ± SD of duration of diabetes was 8.52 ±2.8 years.In case of fungal pneumonia 80% (4) patients had diabetes for more than 10 years and 20% (1) patients had duration between 5- 10 years. Mean duration of diabetes in fungal pneumonia was 13.5 ± 9.7 years.From the Fig 4. 26.92% patients were smoker and 29.81% patients were alcoholic in pneumonia patients. In cases of fungal pneumonia 2 (40%) patients had history of smoking and 2 (40%) patients were alcoholic.

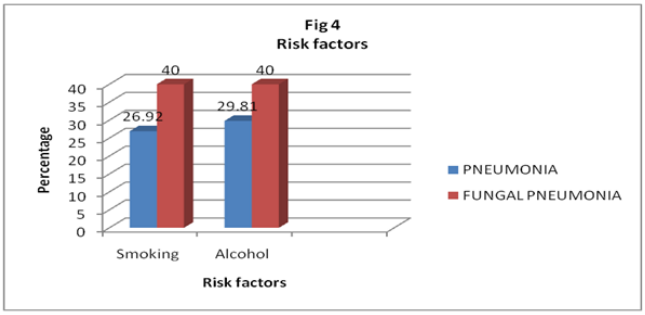


Fig. 4: Risk Factors of Pneumonia and Fungal Pneumonia Cases

Table 3: Relationship With Glycemic Status

| PARAMETERS | PNEUMONIA | | | | FUNGAL PNEUMONIA | | | |
|---|---|---|---|---|---|---|---|---|
| | MEAN | ± S.D. | RANGE | | MEAN | ± S.D. | RANGE | |
| | | | *Min* | *Max* | | | *Min* | *Max* |
| FBS | 218.48 | 45.72 | 99.00 | 431.00 | 243.65 | 48.72 | 143.00 | 431.00 |
| PPBS | 306.16 | 97.05 | 123.00 | 546.00 | 398.16 | 57.67 | 223.00 | 546.00 |

From the table 3. it is observed that mean ± SD FBS was 218.48 ± 45.72, PPBS was 306.16 ± 97.05 .In case of fungal pneumonia Mean ± SD FBS was 243.65 ± 48.72, Mean ± SD PPBS was 398.16 ± 57.67.

Table 4: Distribution Of Patients In Relation To HbA1c Level

| HBA1c | PNEUMONIA | | FUNGAL PNEUMONIA | |
|---|---|---|---|---|
| | Total Number *(n=104)* | Percentage *(%)* | Total Number *(n=5)* | Percentage *(%)* |
| <7% | 9 | 8.65 | 0 | 0 |
| 7%–8% | 12 | 11.54 | 0 | 0 |
| >8%–9% | 31 | 29.81 | 0 | 0 |
| >9%–10% | 32 | 30.77 | 2 | 40.00 |
| >10% | 20 | 19.23 | 3 | 60.00 |
| *Mean ± S.D.* | 9.19% ± 1.85% | | 11.43% ± 2.78 | |

From the above table 4. it was observed that 30.77% pneumonia patients had HbA1C level in the range of >9-10 % and 19.23% patient had above 10%. Only 8.65% patient had HBA1c less than 7%. The mean HbA1C was 9.19 ± 1.85%. But in fungal pneumonia 40% had HbA1c level in 9-10 % range and most of the patients (60%) were in > 10 % of HbA1c range.

Table 5: Sputum Culture Results In The Study Population

| CULTURE REPORT | | NUMBER (n=104) | PERCENT (%) |
|---|---|---|---|
| Fungal Culture | Significant growth of Candida species | 33 | 31.73 |
| | Significant growth of Aspergillus species | 04 | 3.84 |
| | No significant growth of other fungus | 67 | 64.42 |
| Bacterial Culture | Significant growth present | 61 | 58.65 |
| | No significant growth | 43 | 41.35 |
| Both Fungal and Bacterial Culture | Significant growth present | 26 | 25.00 |
| | No significant fungal or bacterial growth | 32 | 30.77 |

From the table 5, out of 104 patients, 37 (35.57%) had significant fungal growth on culture, out of which cases 33 (31.73%) had significant growth of Candida and 4(3.84%) patient had significant growth of Aspergillus. Total number of significant bacterial growth was 61 (58.65%). Among them, 26 (25.00%) had significant growth of both fungi and bacteria in culture. 32 (30.77%) cases had neither fungal nor bacterial growth.

Table 6: Different Fungal Species Causing Pneumonia in Diabetes

| Fungal Culture Report | PNEUMONIA | | FUNGAL PNEUMONIA | |
|---|---|---|---|---|
| | Total Number *(n=104)* | Percentage *(%)* | Total Number *(n=05)* | Percentage (%) |
| Significant growth of Candida species | 33 | 31.73 | 1 | 20.00 |
| Significant growth of Aspergillus species | 04 | 3.84 | 04 | 80.00 |

From the table 6, it was observed that out of total cases of 104, 33 (31.73%) had culture positive for Candida from which only one (0.9%) caused pneumonia and in 4 species of Aspergillus identified all 4 (3.84%) were found to be causing pneumonia. Out of total 5 cases of fungal pneumonia, 1 (20.00%) was caused by Candida and 4 (80.00%) were caused by Aspergillus.

Table 7: Sputum Fungal Culture Showing Different Types of Fungus in Pneumonia in Diabetes

| Species | Number(N=37) | Percentage (%) |
|---|---|---|
| Candida albicans | 23 | 62.16 |
| Candida glabrata | 2 | 5.40 |
| Candida krusei | 1 | 2.70 |
| Candida tropicalis | 2 | 5.40 |
| Other Candida spp. | 5 | 13.51 |
| Asp. Fumigates | 02 | 5.40 |
| Aspergillus flavus | 02 | 5.40 |
| TOTAL | 37 | 100 |

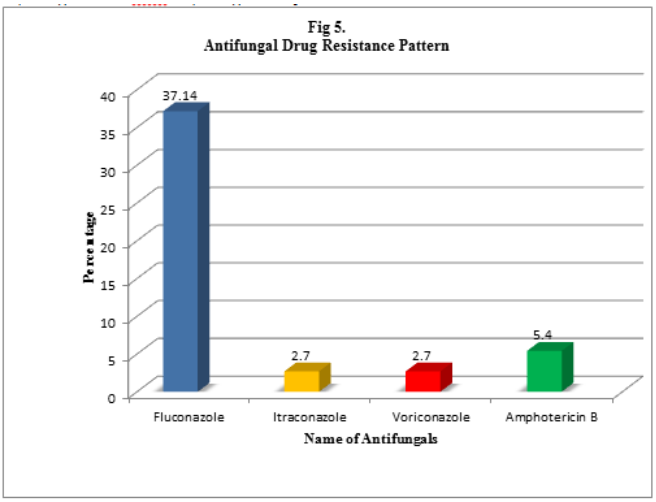


Fig 5: antifungal drug resistance pattern in pneumonia in diabetes

Fig. 5 shows among 37 different species of fungus, drug resistance was found for fluconazole in 13 (37.14%), itraconazole in 1 (2.70%), voriconazole in 1 (2.70%) and amphotericin B in 2 (5.40%).

Table 8: Individual Drug Sensitivity Reports For Each Fungus

| Name of the fungus | Total number of growth (n = 37) | Resistance to anti fungal drugs | | | |
|---|---|---|---|---|---|
| | | Fluconazole | Itraconazole | Voriconazole | Amphotericin B |
| *Candida albicans* | 23 | 7 | 1 | 0 | 1 |
| *Candida* | 2 | 2 | 0 | 0 | 0 |

| | | | | | |
|---|---|---|---|---|---|
| *glabrata* | | | | | |
| *Candida krusei* | 1 | 1 | 0 | 0 | 0 |
| *Candida tropicalis* | 2 | 1 | 0 | 1 | 1 |
| Other *Candida spp.* | 5 | 1 | 0 | 0 | 0 |
| Aspergillus fumigatus | 2 | 0 | 0 | 0 | 0 |
| Aspergillus flavus | 2 | 1 | 0 | 0 | 0 |

From the table 8. among the 23 Candida albicans, anti-fungal drug resistance was observed with fluconazole in 7 (30.43%) cases, itraconazole in 1 (4.34 %), voriconazole 0 (0%) and amphotericin B 1 (4.34 %).Among the 2 Candida glabrata, fluconazole resistance in 2 (100%) whereas 0 (0%) for itraconazole, voriconazole and amphotericin B.For Candida krusei, anti-fungal resistance was observed only with fluconazole and for Candida tropicalis culture positive patients, fluconazole in 1 (100%) and 0 (0%) for itraconazole, voriconazole and amphotericin B.Among 5 other Candida species culture positive patients, only 1 case was resistant to only fluconazole. In case of 4 Aspergillus species antifungal resistance was found only in 1 (25%) to fluconazole.

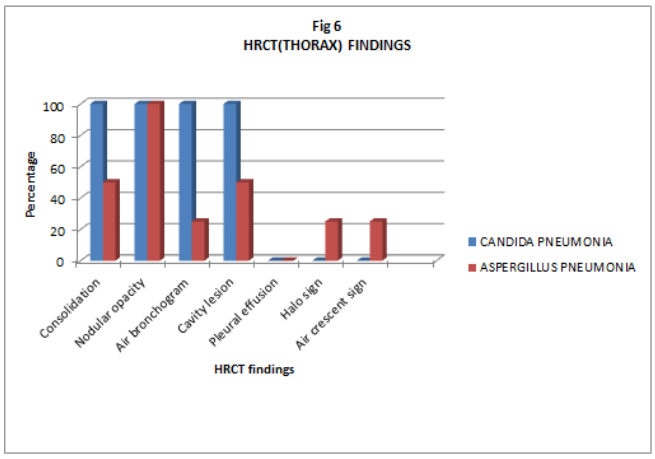


Fig 6: HRCT Thorax Findings In Fungal Pneumonia

5 cases of fungal pneumonia, one (100 %) case of Candida had cavitary lesion with consolidation ,nodular opacity and air bronchogram on imaging. In cases of fungal pneumonia caused by Aspergillus, nodular opacity in 4(100%), consolidation in 2 (50%) cases and air bronchogram was seen in 1 (25%) case on imaging. 2 (50%) cases were found to have cavity on imaging. 1 (25%) case was found to have halo sign and one case (25%) had air crescent sign on HRCT scan of thorax.

**Discussion**

**Age Distribution:** From our study majority of the cases (30.70%) were in the age group of 61-70 years, followed by 23.07% in the age group 51-60 years. In age group >12 - 20 had 0.96% of patients. The mean ± SD age group in the study was 57.01 ± 15.56 years.

This finding was in accordance with sammaiah *et al* (2018)[19] where the incidence appeared to be greatest between 40 and 60 years. The minimum age in our study was 17 years and maximum age was 96 years.

Chandra N *et al.*(2017)[20] found the mean ± SD age 58 ± 26.7(range 13-88 years) in their study .

Out of 5 cases of fungal pneumonia, 4 cases occurred above 60 years of age and one case was seen in 41-50 years bracket. Mean age for fungal pneumonia was 66.20 ± 8.56 years.

Agusti *et al.*(2006)[21] in their study found that the mean age for fungal pneumonia was 68 ± 9 years. The findings are similar to our present study.

**Sex Distribution:** In our study, we encountered males 61.54% and female 38.46% in pneumonia and the ratio between male and female was 1.65:1. Out of the 5 cases of fungal pneumonia 3 (60%) were male and two (40%) were female with male to female ratio 1.5:1.

Sammaiah P *et al*(2018)[19] found male predominance with 80% male and 20% female cases.

Agusti C. *et al* (2006)[21] in a study ,out of 7 cases they encountered 5 male and 2 female cases.

Chen K. *et al* (2001)[22] in their study, found fungal pneumonia in 58.57% patients where female comprised 41.42% cases.

**Clinical Presentation:** In our study, pneumonia patients presented with fever (100%), cough (77.89%), chest pain (39.42%), breathing difficulty (70.19%), hemoptysis (10.57%) and 4.81% patients had weight loss.

Yacovo S *et al.* (2013)[23] encountered fever(38.5%), cough(79.5%), dyspnea(64.5% ) and chest pain(29% ) patients in their study .

In our study, fungal pneumonia had similar presentation with 100% patients having cough and fever. Haemoptysis in 40% and weight loss in 80% cases both of which are more common in fungal pneumonia.

Agusti C et al.(2006)[21] in their study found that 100% of the patients of fungal pneumonia presented with fever.

**Duration of Symptoms:** In our study it was observed that most (75.96%) of the pneumonia patients had symptoms duration less than 7 days. 19.23% patients had 7 to 21 days and 4.81% of the patients had symptoms duration more than 3 weeks. Mean ± SD duration at presentation was 5.39 ± 5.05 days.

In case of fungal pneumonia mean duration of presentation was 21.59 ± 9.73 days.

Agusti C et al.(2006)[21] in their study found that duration of symptom before presentation in fungal pneumonia was 13 ± 9 days.

**Duration of Diabetes Mellitus:** From our study it was observed that most of the pneumonia patients (50%) had diabetes for duration of 5- 10 years and 27.88% patients had diabetes for duration of 5 years or less before presenting to our department.22.12% patients had diabetes for more than 10 years duration. In the patients diagnosed with fungal pneumonia, 20% patients had diabetes for less than 10 years and 80% (4 patients) had diabetes for more than 10 years. Mean duration of diabetes at presentation in cases of fungal pneumonia was 13.5 ± 9.7 years.

**Risk Factors:** Our study shows that 26.92% of the pneumonia patients were smoker and 29.81% patients were using regular alcohol. In the patients with fungal pneumonia the same was found to be 2 (40%) were alcoholic and 2 (40%) were smoker.

The study by sammaiah et al.(2018)[19] showed that 20.5% patients to be smoker and 6.7% patients were alcoholic.

Yacovo S et al.(2013)[23] in their study found that 15.1 % patient were smoker and 12.4% patient were alcoholic.

**Fasting Blood Glucose:** In our present study, mean fasting blood glucose in pneumonia was found to be 218.48 ± 45.72 mg/dl. (range 99-431). In case of fungal pneumonia Mean fasting Blood glucose was 243.65 ± 48.72(range 143-431).

Chandra et al.(2017)[20] in their study observed mean fasting blood glucose as 230.9 ± 75.3 (range 136-442).

**Post Prandial Blood Glucose:** In our present study the mean post prandial blood glucose in pneumonia was found to be 306.16 ± 97.05 mg/dl (range 123-

546mg/dl). In case of fungal pneumonia mean post prandial blood glucose was found to be 398.16 ± 57.67 mg/dl (range 223-546mg/dl).

Chandra et al.(2017)[20] in their study found mean post prandial blood glucose 349±109.5 mg/dl (range 236-500).

**HbA1c Status:** From our present study it was observed that 30.77% pneumonia patient had HbA1C level in the range of >9-10 and 19.23% patient had this value above 10%. Only 8.65% patient had HBA1c less than 7%. The mean HbA1C was 9.19 ± 1.85 %. In case of fungal pneumonia all had HbA1C level above 9%.

Chandra et al.(2017)[20] in their study found the mean HbA1C to be 9.3% ± 2.5 (range 6.2%-15.5%)

**Sputum Culture:** In our present study out of 104 patients, 33 (31.73%) had significant growth of Candida and 4 (3.84%) patient had significant growth of Aspergillus. Total number of significant bacterial growth was 61 (58.65%). Among them, 26 (25.00%) had significant growth of both fungi and bacteria in culture. 32 (30.77%) cases had neither fungal nor bacterial growth.

Out of 37(35.5%) significant fungal species isolated, Candida albicans was 23 (62.16%), Candida glabrata 2 (5.40%), Candida krusei 1 (2.70%), Candida tropicalis 2 (5.40%) and other Candida species 5(13.51%). In 2(5.40%) cases Aspergillus flavus and in 2 (5.40%) cases Aspergillus fumigatus was isolated.

Phukan AC et al (2000)[24] in a study of bronchopulmonary candidiasis in Assam Medical College, Assam found that pulmonary candidiasis was associated with chronic bronchitis in 37.8% of cases. The study revealed 6 different species of Candida associated with chronic bronchopulmonary diseases, out of which Candida albicans were most frequently (76%) isolated, followed by Candida tropicalis (10%) and others.

**Antifungal Susceptibility Test Of The Fungal Species:**

In our study among these 37 different species, drug resistance was found for fluconazole in 13 (37.14%), itraconazole in 1 (2.70%), voriconazole in 1 (2.70%) and amphotericin B in 2 (5.40%).

Among the 25 Candida albicans, anti-fungal drug resistance was observed with fluconazole in 7 (28.00%) cases, itraconazole in 1 (4.00%), voriconazole 0 (0%) and amphotericin B 1 (4.00%); among the 2 Candida glabrata, fluconazole in 2 (100%), itraconazole in 0 (0%), voriconazole in 0 (0%) and amphotericin B in 0 (0%); among the 1 Candida krusei, anti-fungal resistance was observed only with fluconazole; among the 1 Candida tropicalis culture

positive patients, fluconazole in 1 (100%), itraconazole in 0 (0%), voriconazole in1 (100%) and amphotericin B in 1 (100%) and among 4 other *Candida species* culture positive patients, only 1 case was resistant to only fluconazole. In case of 4 Aspergillus species antifungal resistance was only found in 1 (25%) to fluconazole.

Songsong Y *et al.*(2016)[25] in their study observed that resistance to fluconazole in all the 3 *Candida glabrata* strain, and itraconazole resistance in 1 of the 3 *Candida glabrata* strain. In all Candida strains, they found resistance to fluconazole in 13.04%, and to itraconazole in 4.35% cases.

The resistance to the antifungal agents was higher in our study. Fluconazole resistance was highest in all groups. It might be due to increasing use of antifungal, being most commonly used for skin infection. Interestingly *Candida tropicalis* showed resistance to fluconazole, amphotericin B and voriconazole. The latter two being uncommonly used drugs. Primary drug resistance may be present to these two drugs.

**Fungal Pneumonia and Imaging:** Out of the 5 cases of fungal pneumonia, one case by Candida had cavitary lesion with consolidation, nodular opacity and air bronchogram on imaging. In cases of fungal pneumonia caused by Aspergillus, 4 (100%) had nodular opacity, 2 (50%) had consolidation, 1 (25%) had air bronchogram and 2 (50%) cases were found to have cavity on imaging. 1 (25%) case was found to have halo sign and air crescent sign on HRCT scan of thorax.

Green *et al.*(2007)[26] in their study had the following findings in case of Aspergillus infection of lung at presentation, most patients (94%) had 1 macro nodules, and many (61%) also had halo signs. Other imaging findings at presentation, including consolidations (30%), infarct-shaped nodules (27%), cavitary lesions (20%), and air-crescent signs (10%), were less common.

**Fungal Pneumonia:** From our study, out of 37 (among 104 diabetics with pneumonia) different species of fungus only 1(0.9%) case of Candida and 4 (3.84%) cases of Aspergillus were associated to be causing fungal pneumonia. We encountered total 5 cases of fungal pneumonia in a period of 1 year.

El-Ebiary *et al.*(1997)[27] in a study ,they found that out of 25 cases where Candida was isolated from biopsy of lung only 2 (8%) had definite pulmonary candidiasis.

Chen K. *et al.* (2001)[22] in their study for a period of 10years (from 1988 – 1997), a total 140 cases of fungal pneumonia were diagnosed. 5 cases in1988, 8 in 1989, and 6 in 1990. There were 10, 11, and 8 cases annually in 1991, 1992, and 1993, respectively. However, there were 15 cases annually from 1994 through 1997 (16 in 1994, 26 in 1995, 20 in 1996, and 30 in 1997), with increase in both nosocomial and community-acquired infections.

**Limitations of the Study:** The limitation of our study that might interfere with the results were: 1)Small sample size 2)Short duration of study 3)Broncho-alveolar lavage samples are better to look for pulmonary pathogens than sputum, but due to lack of cooperation of patients and for ethical consideration only sputum culture was done.

**Conclusion**

Our study showed that fungal pneumonia was not uncommon in patient with diabetes especially in diabetics with poor glycemic control. The results obtained in our study are a good indicator showing proportions of respiratory fungal infection and prevalence of fungal pneumonia in diabetics in this part of our country. However, more studies with larger population and longer duration are required in order to explore other aspects which will help treating physician to provide better management options to the patients.

**References**


1. Tarsia P. 100 years of respiratory medicine: Pneumonia. Respiratory Medicine 2007;101:875–81.
2. The World Book Encyclopedia of Science (The Plant World Book). A World Book Inc, Chicago. 1994; 28-29.
3. Mohapatra LN, Pande JN. Pulmonary Mycotic Infections. In: Ahuja MMS, Ed. Progress in Clinical Medicine in India, Heinemann A. New Delhi 1978; 23539.
4. Seaton A, Seaton 0, Leitch AG. Fungal and Actinomycotic Diseases. In: Crofton and Douglas's Respiratory Diseases 4th Ed. Oxford University Press Delhi 1989; 448-475.
5. Fraser RS, Pare JAP, Eraser RG, Pare PD. In: Infectious Diseases of Lungs in Synopsis of Diseases of Chest 2nd Ed. WB Saunders & Co; Philadelphia: 1994; 332-54.
6. Limper AH, Knox KS, Sarosi GA, Ampel NM, Bennett JE, Catanzaro A, Davies SF, Dismukes

WE, Hage CA, Marr KA, Mody CH. An official American Thoracic Society statement: treatment of fungal infections in adult pulmonary and critical care patients. American journal of respiratory and critical care medicine. 2011 Jan 1;183(1):96-128.

7. Kornum JB, Thomsen RW,Riis A, Lervang HH, Schonheyder HC, Sorensen HH. Diabetes, Glycemic Control, and Risk of Hospitalization With Pneumonia: A population-based case-control study. Diabetes Care.2008 Aug;31(8):1541-5
8. Sammaiah P, Prasad R, Shekhar VC. Study of Bacteriological and Clinical Profile of Community Acquired Pneumonia in Type 2 Diabetes Patients in Tertiary Care Hospital, Warangal. Int J Sci Stud 2018;6(3):130-134.
9. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2019. Diabetes Care. 2018;42(Supplement 1).
10. British Thoracic Society guidelines for the management of communtity-acquired pneumonia in adults: update 2009. Thorax 2009;64(Suppl III):iii1–55.
11. De Pauw B, Walsh TJ, Donnelly JP, Stevens DA, Edwards JE, Calandra T, et al . Revised definitions of invasive fungal disease from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) Consensus Group. Clin Infect Dis. 2008 Jun 15;46(12):1813-21
12. Chander J. Text Book of Medical Mycology. 3rd edition. New Delhi: Mehta Publishers; 2009.p.53-62.
13. Protocol for processing specimens for culture[Internet]. Tbcare1.org. 2016 [cited 26 Jun 2019]. Available from: http://www.tbcare1.org/publications/toolbox/tools/dst/participant_manual/Module_6_2_Annex_6.1.doc.
14. Kapil A, Bhaskaran CS, editors. Ananthanarayana&Paniker's, editors. Textbook of microbiology. 9th ed. Hyderabad: Universities Press (India) Private Limited; 2013. p.589-615.
15. Tille PM. Bailey & Scott's diagnostic microbiology. 13th ed. St.Louis, Missouri: Elsevier 2014. p.742-43.
16. Collee JG, JP Duguid Fraser AG, Marmion BP, Simmons A. Laboratory strategy in the diagnosis of infective syndrome. Mackie and McCartney practical medical microbiology (english). 14th ed. South Asia: Elsevier Health Sciences; 2014. p.63.
17. Phadke SN, Katare SN, Gupta JC, Vyas GR. Study of fungi associated with chronic broncpulmonary diseases. Indian J Path Microbial 1979 Oct:22(4):381-387.
18. Biswas D, Agarwal S, Sindhwani G, Rawat J. Fungal colonization in patients with chronic respiratory diseases from Himalayan region of India. Annals ofClinical Microbiology and Antimicrobials. 2010 Sep 20;9(1):28.
19. Sammaiah P, Prasad R, Shekhar VC. Study of Bacteriological and Clinical Profile of Community Acquired Pneumonia in Type 2 Diabetes Patients inTertiary Care Hospital, Warangal Warangal. Int J Sci Stud 2018;6(3):130-134.
20. Chandra N, Subhalaxmi MVS, Umabala P, Raju YSN. Incidence of infection in hospitalized subject with diabetes mellitus. J Clin Sci Res 2017;6:216-24.
21. Agustí C, Rañó A, Aldabó I, Torres A. Fungal pneumonia, chronic respiratory diseases and glucocorticoids. Med Mycol. 2006;44(SUPPL. 1):207–11.

22. Chen KY, Ko SC, Hsueh PR, Luh KT, Yang PC. Pulmonary fungal infection: Emphasis on microbiological spectra, patient outcome, and prognostic factors. Chest [Internet]. 2001;120(1):177–84.
23. Yacovo S Di, Garcia-vidal C, Viasus D, Adamuz J, Oriol I, Gili F. Clinical Features , Etiology , and Outcomes of Community-Acquired Pneumonia in Patients With Diabetes Mellitus. 2013;92(1):42–50.
24. Phukan AC, Sarmabardoloi JN, Mahanta J.Bronchopulmonary candidiasis in a tertiary referral hospital of Assam India.Ind J Med Sci. 2000; 54: 491-4.
25. Songsong Y, Qiuhong F. Analysis of the Etiological Distribution and Drug Resistance of Pathogens in Hospitalized Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease. Chest. 2016;149(4):A362.
26. Greene RE, Schlamm HT, Oestmann JW, Stark P, Durand C, Lortholary O, Wingard JR, Herbrecht R, Ribaud P, Patterson TF, Troke PF. Imaging findings in acute invasive pulmonary aspergillosis: clinical significance of the halo sign. Clinical Infectious Diseases. 2007 Feb 1;44(3):373-9.
27. El-Ebiary M, Torres A, Fàbregas N, De La Bellacasa JP, González J, Ramirez J, et al. Significance of the isolation of Candida species from respiratory samples in critically ill, non-neutropenic patients: An immediate postmortem histologic study. Am J Respir Crit Care Med. 1997;156(2 I):583–90.