“ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST”

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the requirements for the degree of

Doctor of Medicine (M.D) in
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Branch – XVII

Institute of Thoracic Medicine,
Madras Medical College &
Rajiv Gandhi Government General Hospital

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BONAFIDE CERTIFICATE

This is to certify that the dissertation titled “ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST” is the Bonafide work done by Dr. PALANIAPPAN C during his M.D (Tuberculosis and Chest Diseases) course in the academic years 2014-2017, at the Institute of Thoracic Medicine and Rajiv Gandhi Government General Hospital – Madras Medical College, Chennai. This work has not previously formed the basis for the award of any degree.

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submitted for the degree of Doctor of Medicine (M.D) in Tuberculosis
and Chest Diseases, Branch XVII is my original work and the dissertation
has not formed the basis for the award of any degree, diploma, associate
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ABBREVIATIONS

TURNITIN-PLAGIARISM SCREEN SHOT

DIGITAL RECEIPT

ETHICAL COMMITTEE APPROVAL ORDER

CONSENT FORM

PROFORMA

MASTER CHART
ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST
INTRODUCTION

The immune compromised host is defined as a person who has an alteration in phagocytes, the humoral or cellular immunity that increases the risk of infectious complication. There is a growing group of individuals apart from ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) who are now immune suppressed like, those receiving immune suppressants for Solid Organ Transplants (SOT), Bone Marrow Transplant (BMT), Connective Tissue Diseases or treated with chemotherapeutic agents for cancer. Widespread use of “Biological Agents”, which are generally antibodies targeting specific cell type or pathway of inflammation, has further expanded the susceptible population.

Managing systemic infections are challenging in such patients among which pulmonary infection is very frequent. The development of pulmonary disease among such patients is considered as a serious problem. The differential diagnosis includes infectious and many non-infectious causes. Given the broad spectrum of potential infections and non-infectious causes, coupled with inherent toxicities of many therapies, a specific microbiological and cytopathological diagnosis should be considered essential to the management of pulmonary infections in non-HIV immune compromised host.

Noninvasive test available can be done easily with less risk, but overall they are of little diagnostic use and their yield is also low. So invasive strategies become essential for management of pulmonary diseases. Among the invasive test Bronchoscopy and Bronchoalveolar Lavage (BAL) has proved to be the procedure with good yield and is well tolerated even in critically ill patients, with
a low complication rate. It also leads to the most appropriate diagnosis. The sensitivity and specificity for diagnosing pulmonary infections is also good. Early diagnosis and appropriate treatment reduces the mortality and increases survival benefits. Hence, early bronchoscopy if possible before starting antibiotic therapy remains crucial in the management of immune compromised host with pulmonary infections.
REVIEW OF LITERATURE

The immune compromised host is defined as a person who has an alteration in phagocytes, the humoral or cellular immunity that increases the risk of infectious complication or an opportunistic process like lymphoproliferative disease or cancer.

J.L. Mahon et al., defines an immunocompromised patient is one with any defect in the immune system and immunodeficiency is applied to any person affected by disease or situations in which the immune system itself, including complement, phagocytes and lymphocytes is impaired.

CENTER FOR DISEASE CONTROL (CDC) for practical purposes, divides immune compromising conditions into 3 broad categories:

A. Persons who are severely immune compromised not as a result of HIV infection;

B. Persons with HIV infection; and

C. Persons with conditions that cause limited immune deficits (e.g., asplenia, renal failure)

SEVERELY IMMUNOCOMPROMISED, NON-HIV-INFECTED PERSONS

1. Congenital immunodeficiency

2. Leukemia, lymphoma, generalized malignancy
3. Therapy with alkylating agents, antimetabolites, radiation, or large amounts of corticosteroids

**MEDICAL CONDITIONS THAT CAUSE LIMITED IMMUNE DEFICIENCY**

1. Renal failure - End stage renal disease is associated with infections which contribute to 20% mortality, which is due to alteration in immune system. Matthias Girndt et al., in his article on the impaired cellular immune function in patients with end-stage renal failure states that patients with chronic renal failure are at increased risk of infections similar to other acquired immune defects. The secondary immune failure is due to uremic intoxication per se and by altered renal metabolism of immunologically active proteins.

2. Alcoholic cirrhosis

3. Asplenia

The IDSA (INFECTIOUS DISEASE SOCIETY OF AMERICA) has defined immune suppression as High & Low level immune suppression.

**HIGHLEVEL IMMUNOSUPPRESSION INCLUDES:**

1. Combined primary immunodeficiency disorder (eg, severe combined immunodeficiency)

2. Receiving cancer chemotherapy

3. Within 2 months after solid organ transplantation
4. With HIV infection with a CD4 T-lymphocyte count <200 cells/mm3 for adults and adolescents and < 15% for infants and children

5. Receiving daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥14 days

6. Receiving certain biologic immune modulators, that is, a tumor necrosis factor-alpha (TNF-α) blocker or rituximab

LOW-LEVEL IMMUNOSUPPRESSION INCLUDES:

1. Asymptomatic HIV-infected patients with CD4 T-lymphocyte counts of 200–499 cells/mm3 for adults and adolescents and 15–24% for infants and children

2. Those receiving a lower daily dose of systemic corticosteroid than for high-level immune suppression for ≥14 days or receiving alternate-day corticosteroid therapy

3. Those receiving methotrexate (MTX) ≤0.4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1.5 mg/kg/day

ETIOLOGY AND DIFFERENTIAL DIAGNOSIS FOR PULMONARY DISEASES IN NON-HIV IMMUNE SUPPRESSED

Includes both infectious & non-infectious etiologies.

Rañó A et al.\(^8\), in his study of pulmonary diseases in non-HIV immuno compromised patients found that 77% of pulmonary diseases were infectious and remaining 23% were non-infectious and among non-infectious causes pulmonary edema and alveolar haemorrhage were most common.
Similarly, Rosenow EC, et al. observed the same differential diagnosis for pulmonary diseases among non-HIV immunocompromised host. In his study he observed 25% of pulmonary diseases were due to non-infectious causes.

Bianca Harris et al., in his focused review on Bronchoscopy in Solid Organ and Haematopoietic transplant patients observed the following differential diagnosis for pulmonary diseases.

**Table 1.** Differential diagnosis of pulmonary disease in non-HIV immuno compromised host

|   |   |
|---|---|
| 1. | Infection |
| 2. | Drug induced pulmonary disease |
| 3. | Recurrence of underlying disease |
| 4. | Pulmonary haemorrhage |
| 5. | Idiopathic fibrosis |
| 6. | "Unrelated" disease |
| 7. | Acute rejection |
| 8. | Malignancy |
| 9. | Pulmonary edema. |
| 10. | Combination of above |

**PULMONARY INFECTIONS IN NON-HIV IMMUNOCOMPROMISED**

Infections are the most common cause of pulmonary diseases. An unilateral, localized process is very likely to be infectious in origin (90%), whereas diffuse disease is somewhat less frequent (75%) \(^{12,13,14}\)

Nimrod Maimon et al., approaches the differential diagnosis of pulmonary infections in two ways, first is to relate the various organisms to defect in primary immune system, the more important second one is to consider the probability of
various organisms in context of different underlying immune defect. According to him the pathogens summarized below account for 90% of opportunistic infections.

Table 2. The most common infectious organisms

| Bacteria          | Fungi                      | Viruses         | Protozoa         |
|-------------------|----------------------------|-----------------|------------------|
| Staphylococcus    | Pneumocystis carinii       | Cytomegalovirus | Toxoplasma gondii|
| Aureus            |                            |                 |                  |
| Streptococcus     | Candida sp.                | Herpes simplex  | Strongyloides stercoralis |
| pneumoniae        |                            |                 |                  |
| Staph. epidermidis| Aspergillus sp.            | Herpes zoster   |                  |
| Pseudomonas       | Histoplasma capsulatum     | Respiratory syncytial virus |
| aeruginosa        |                            |                 |                  |
| Escherichia coli  | Blastomyces dermatitidis  | Influenza A     |                  |
| Legionella        | Coccidioides immitis       | Enterovirus     |                  |
| Nocardia          | Cryptosporidium neoformans|                 |                  |
| Mycobacteria sp.  |                            |                 |                  |

Bacterial, fungal, viral, and mycobacterial pathogens may infect the lungs of immunosuppressed patients. In a prospective series by Rano et al., among 200 non-HIV immunocompromised patients, infectious agents were recovered from more than three fourth of subjects. An etiological diagnosis was obtained in 81% with 19% no diagnosis. Among the 81%, infections were 77% and non-infectious causes contributed to 23%. Among infections bacterial was predominant with
23%, followed by fungal with 17% and viral with 10%. According to Andrew F. Shorr, MD et al., the most common bacterial organisms are nosocomial organisms like Pseudomonas and MRSA. Aerobic Gram-negative bacilli such as Klebsiella pneumonia may also lead to pneumonia.

**SPECTRUM OF PULMONARY FUNGAL INFECTIONS**

Aspergillus infection remains the most common cause of fungal pneumonia. *Aspergillus* species have emerged as important causes of morbidity and mortality in immunocompromised patients. Among the *Aspergillus* species, *Aspergillus fumigatus* is the most common species recovered.

Paterson DL, et al. found Aspergillus infection occurs in 1 to 8% of patients undergoing various solid organ transplants (SOTs) and Hematopoietic stem cell transplants (HSCTs). Chest pain, dyspnea, and hemoptysis are the classical presenting symptoms. Some patients initially have no symptoms.

Jantunen et al. in his series on invasive and probable fungal infections among bone marrow transplant recipients observed Aspergillus was the most frequent cause and only 50% had chest symptoms, 32% had fever and remaining were asymptomatic. The triad of symptoms of chest pain, hemoptysis, dyspnea can occur in pulmonary embolism leading on to confusion in diagnosis. The chest radiograph may initially be normal in up to 10% of cases. Hence, early use of CT scan is necessary. An area of low attenuation may arise next to areas of consolidation referred as halo sign. But it is not specific and is also a late finding. Infections due to other angioinvasive filamentous fungi, such as
Zygomycetes, *Fusarium* species, and *Scedosporium* species, as well as to *Pseudomonas aeruginosa* and *Nocardia* species, may cause a halo sign.\textsuperscript{16}

Calliot D, et al\textsuperscript{14}, in his study of definitive Aspergillus cases, the sensitivity of halo sign was only 50%. The yield of bronchoscopy for aspergillosis in immune suppressed patients is approximately 50%.

FREDERICK W. KAHN et al \textsuperscript{18}, in his study of 82 immunocompromised patients undergoing bronchoscopy for pulmonary infiltrates found that Aspergillus hyphae was found 9 out 17 cases with invasive aspergillosis. BAL had a sensitivity of 53% and specificity of 97% and positive predictive value of 75% as per his study. Thus he concluded that BAL was a valuable procedure for diagnosing invasive aspergillosis. The newer techniques like galactomannan assay has sensitivity 80-90% and specificity > 95%.\textsuperscript{19,20}

The other important fungi that cause pneumonia in immunocompromised patients are endemic mycosis *Histoplasma capsulatum*, *Coccidioides immitus*, and *Blastomyces dermatitidis*\textsuperscript{15}.

Candida though often isolated from respiratory tract of immunocompromised patients rarely cause pneumonia except in lung transplant recipients\textsuperscript{15}. Haron E et al\textsuperscript{21}, in his study identified primary candida pneumonia in only 0.4% of autopsies at the M.D. Anderson Cancer Center. Since the isolation of Candida often represents colonization rather than true infection attributing pulmonary infiltrates to Candida pneumonia is difficult. Demonstration of tissue invasion by transbronchial or surgical lung biopsy is required for definitive diagnosis. But
even though Candida is frequently a colonizer, Respiratory tract Candida colonization is associated with worse clinical outcomes and is independently associated with increased hospital mortality \(^{22,23}\).

**PNEUMOCYSTIS CARINII PNEUMONIA**

Yale SH, et al \(^{24}\), found in his study up to 90% of Pneumocystis carinii pneumonia occur in patients treated with steroids within 4 weeks of diagnosis. He found the mean corticosteroid dose was 30mg/day and mean duration of steroid therapy was 12 weeks before the development of pneumonia.

Pneumocystis carinii pneumonia also has been linked directly to Fludarabine therapy for CLL \(^{25}\). The radiological pattern tends to be bilateral with fine Perihilar or small nodular infiltrates.

BAL has a very good yield for PCP. The BAL yield for PCP with conventional stain is 80% in non-HIV & 95% in HIV patients \(^{26}\)

**PREVALENCE OF PULMONARY TUBERCULOSIS**

The incidence of tuberculosis varies depending on the underlying cause for immunosuppression. In areas where Tuberculosis is highly prevalent the possibility of tuberculosis is high.

Jane C. Chan et al. \(^{27}\), in his study in Hong Kong among 62 Non-HIV immunocompromised found that tuberculosis was the second most common cause of pulmonary infections after bacterial infections. The incidence of tuberculosis was 19%. The overall bronchoscopic sensitivity for tuberculosis
was 91%. The radiographic presentation was nonspecific. Hence in countries where there is high prevalence of tuberculosis, bronchoscopy should be utilized readily for smear negative cases in immunocompromised patients and empirical treatment may be started awaiting culture results.

**NON-INFECTIONIOUS ETIOLOGIES**

There are various non-infectious causes of pulmonary diseases in immunocompromised. Upto 25% of pulmonary diseases in immunocompromised can be attributed to non-infectious causes. Some of the non-infectious causes can have a poorer prognosis.

**PULMONARY EDEMA**

Pulmonary edema is one of the common non-infectious causes of pulmonary disease. Andrew F. Shorr et al, states that the causes of pulmonary edema include,

1. Hydration prior to chemotherapy for leukemia.
2. Volume overload status in chronic kidney disease patients and sometimes post renal transplant patients.
3. Chemotherapeutic agents like doxorubicin induced cardiotoxicity.
4. Indirect causes like drugs, radiation, sepsis, that promotes lung injury and capillary leak.

Patients have diffuse pulmonary infiltrates predominantly involving lower lobes and are afebrile. Some patients can even decompensate quickly, but respond to
treatment well and the prognosis is good. Hence extreme care needs to be taken while assessing the fluid status of immunocompromised patients.  

**RECURRENCE OF UNDERLYING DISEASE**  

In patients with underlying malignancy the disease progression may result in the development of pulmonary disease. The infiltrates may be discrete nodules, masses, diffuse alveolar infiltration as seen in lymphomas or lymphangitic pattern with interstitial involvement may also occur. Bronchoscopy helps to rule out infections and helps to get the tissue biopsy needed to prove the diagnosis.  

**DRUG INDUCED PULMONARY DISEASE**  

Many drugs are associated with pulmonary toxicity. Some like Busulfan are directly implicated in causing pulmonary disease. Pathological patterns of drug induced lung disease may be in the form of diffuse alveolar damage (DAD), granulomatous reactions, and nonspecific pneumonitis. The diagnosis of drug induced lung damage is made clinically,  

1. The temporal relationship between the use of a particular agent and the subsequent development of symptoms  
2. Improvement in pulmonary function after withdrawal of the agent  
3. Exclusion of infection  

Some common drugs associated with pulmonary toxicity include Busulfan, Cyclophosphamide, Methotrexate, Azathioprine, Bleomycin etc...
RADIATION INDUCED LUNG INFILTRATES

Radiotherapy for malignancies can involve the lungs. They result in acute pneumonitis or more slowly, progressive pulmonary fibrosis. Following a dose of radiation to the lungs >2000 rads, radiation injury may be seen. The acute form of radiation pneumonitis may present as bronchitis or esophagitis, with dry cough, fever, fatigue, hypoxemia, and dyspnea that develop over 6 to 12 weeks. Radiation fibrosis usually occur in 6 to 9 months, and pulmonary function may take up to 2 years to plateau. Radiation injury may follow a unique pattern on CT chest. The lesions are sharply defined and bounded. They do not follow the anatomic border.

DIFFUSE ALVEOLAR HAEMORRHAGE

Diagnosed by bloodier return from BAL and the presence of hemosiderin laden macrophages. If 20% of the alveolar macrophages are hemosiderin laden, then DAH is present. Radiography shows diffuse alveolar infiltrates in middle and lower lung fields. The incidence ranges from 2 to 14%. The pathogenesis of DAH is unclear. DAH likely arises following an initial lung injury from either chemotherapy or irradiation that results in endothelial damage. Treatment consists of high-dose corticosteroids. Dosages used have ranged from 500 mg to 2 g per day of IV Methylprednisolone.

MORBIDITY AND MORTALITY OF PULMONARY INFECTIONS

Pulmonary complications remain one of the most common causes of morbidity and mortality. Nimrod Maimon MD, et al., in his review article states that the
lungs are involved in at least 75% of immunocompromised patients with any complication. Mortality rate ranges widely from 15%-90%, depending on the underlying disease, the severity of lung involvement, and the total impairment of host defenses.\textsuperscript{11} The development of pulmonary disease in immunosuppressed patients is a diagnostic challenge\textsuperscript{11}

Poe RH et al\textsuperscript{31}, in his study on Predictors of mortality in the immunocompromised patient with pulmonary infiltrates found a mortality rate of 36%. Rañó A et al\textsuperscript{32}, in his study on 200 non-HIV immunocompromised patients found an overall mortality rate of 39%.

These studies show the need for rapid and quick evaluation of pulmonary disease in immunocompromised patients to prevent mortality.

**ROLE OF FOB IN DIAGNOSTIC EVALUATION OF PULMONARY INFECTIONS IN NON-HIV IMMUNOCOMPROMISED HOST**

Pulmonary diseases in non-HIV immunocompromised patient have a variety of differential diagnosis. Apart from infections different non-infectious causes are also predominant

A Rano et al\textsuperscript{8}, in his study on 200 non-HIV immunocompromised patients observed that, in infectious causes when appropriate treatment was changed earlier $< 7$ days had a better outcome (29% mortality) than treatment changed later (71% mortality). This study highlights the importance that the quick evaluation and treatment modification reduces the mortality
A Similar finding was also observed by DANÉS et al.,33 in immunocompromised patients where bacterial pneumonia was most common followed by fungal and viral pneumonias. In his study bacterial pneumonia was associated with unilateral and alveolar type of infiltrates. BAL had a diagnostic yield of 52%. Staph aureus was the most common bacterial pathogen and Aspergillus was most common fungal isolates.

FREDERICK W. Kahn et al.,34 in his study on 94 immunocompromised patients where 100 BAL procedure was done found bronchoscopic yield of 81% for infections. The non-infectious causes observed were malignancy, haemorrhage, pulmonary edema, radiation fibrosis etc. The yield with BAL was similar to that of Trans Bronchial biopsy.

S SHAWGI et al 35., in a study done on 25 patients with hematological malignancies in INDIA found that overall yield was high with 84%. Bacterial pneumonia alone accounted for 40% and 40% polymicrobial, fungal alone remaining 4%. Pseudomonas was most common bacteria and Aspergillus fumigatus was most common fungi isolated. The therapeutic utility was 24%.

PITFALLS OF EMPERICAL TREATMENT

More often clinicians treat patients empirically. The mortality may be high if empirical treatment is not modified early once the patient does not improve 8. It is not possible to cover all diagnostic aetiologies by empirical treatment. Moreover, empiric treatment purely based on clinical criteria alone would be unacceptable given the toxicity associated with such treatment options in most
circumstances. Many of the non-infectious aetiologies are unnecessarily treated with antimicrobials contributing to drug resistance and toxicity. Also, most non-infectious causes are also potentially fatal if not diagnosed and treated correctly. Finally, many non-infectious conditions like DAH may require corticosteroids for their management, which may exacerbate the underlying pulmonary infections if not ruled out properly. Hence ruling out infections thoroughly is mandatory before starting corticosteroid therapy for management of non-infectious causes and also for continuing immunosuppressive therapy.11

Infections in immunocompromised hosts often present without the expected signs and symptoms of infection. Many non-infectious cause like DAH, radiation pneumonitis, malignancy may also present with fever mimicking infections. Hence clinicians must follow an aggressive approach and must have a low threshold for performing investigations when encountered with an immunocompromised patient with pulmonary diseases. Invasive studies such as bronchoscopy or biopsy are best performed early in the course of possible infection and prior to the initiation of antimicrobial therapy.36

DRAWBACKS OF NON-INVASIVE TECHNIQUES

The non-invasive diagnostic methods include serologic tests, blood antigen detection, nasopharyngeal wash, sputum, and tracheobronchial aspirate cultures, chest radiograph, CT chest, sputum AFB staining, Grams staining, Skin tests etc. Though blood cultures are done routinely, they have a low diagnostic yield.
A Rano et al\textsuperscript{8}, in his study found that yield of blood culture was only 16\% & sputum culture with 30\%. Bronchoscopic yield was 59\%. Thus he concluded that BAL had a higher diagnostic yield and impact on therapeutic decisions. Also Sputum culture is valuable only when the organisms not routinely found in oropharyngeal secretions are isolated like mycobacteria, Mycoplasma etc\textsuperscript{11}. 

Danes et al\textsuperscript{33}, in his study found that non-invasive technique like sputum culture was associated with low yield of only 20\%, blood culture with 8\%, and nasopharyngeal wash for viral antigen detection was only 6\%, compared to bronchoscopic yield of around 66\%.

Though standard chest radiograph can be used as a screening tool in immunocompromised patients with chest symptoms, studies have advocated early use of CT scans. A study in renal transplant recipients showed that though chest radiograph was initially normal in patients with pulmonary complaints subsequent CT scan demonstrated abnormalities\textsuperscript{37}. Heussel et al\textsuperscript{38}, in a study on 87 patients with febrile neutropenia found that in 50\% patients CT revealed lesions that were not visualized by chest radiography. Thin section CT was able to detect pneumonia 5 days earlier compared to chest radiograph. CT in addition to identifying lesion missed on chest radiography helps to guide invasive diagnostic procedures like BAL, TBLB etc.

Even though the non-invasive diagnostic techniques are safe and relatively low cost studies have shown that they add little useful information\textsuperscript{8,11,39}. The overall diagnostic yield of non-invasive techniques ranges from 10\%-30\% \textsuperscript{8,33}. 

\textsuperscript{17}
Hence, due to varied aetiology of pulmonary diseases along with non-specific nature of clinical and radiological presentation coupled with low yields of non-invasive techniques makes invasive diagnostic procedures mandatory. The benefit to risk ratio is an important consideration when choosing an invasive procedure in immunocompromised patients who are already critically ill due to the underlying disease. The invasive procedure with good yield and low risk in most of the studies is BAL.\textsuperscript{11,40,41} Lavage is safe, minimally invasive, reproducible and leads to a quick diagnosis. Suitable even for very sick and critically ill patients with less complications. The yield of BAL is better than of Protected brush Sampling, although PBS is more specific.\textsuperscript{42,43}

Jennifer A Crockett, MD et al \textsuperscript{42}, in his study found that yield of BAL was 38% compared to PBS with 10% and TBB with 27%. Adding BAL, PBS, Transbronchial biopsy during the bronchoscopic procedure increases the diagnostic yield, sensitivity and specificity at the same time complication rate of the procedure \textsuperscript{43}.

Rano et al \textsuperscript{8}, in his study found that BAL had the best diagnostic yield of 51%, better than PBS (24%), with only 3 minor complications and led to treatment modification in 38%.

Gruson D et al \textsuperscript{44}, studied the role of bronchoscopy in the management of pulmonary infiltrates in neutropenic patients found that BAL had a complication rate of 17% and acceptable yield of 49%.
AIMS AND OBJECTIVES

PRIMARY OBJECTIVES

- To study the diagnostic yield of bronchoscopy modification of current empirical treatment as the result of bronchoscopic intervention.

among NON-HIV immunocompromised patients presenting with pulmonary diseases in a tertiary care center.

SECONDARY OBJECTIVES:

- To collect data on etiology of different microorganisms among Non-HIV immunocompromised patients.
- To collect data on non-infectious causes of pulmonary diseases in Non-HIV immunocompromised patients in our tertiary care center.
- Compare symptoms at the time of presentation, with bronchoscopic yield.
- Compare the different radiological pattern, with bronchoscopic yield.
- Compare different subgroups of Non-HIV immunocompromised patients with regards to presenting symptoms, radiological patterns, bronchoscopic yield, treatment modification, different spectrum of infections & complications.
MATERIALS & METHODS

STUDY CENTER

The study was conducted in Rajiv Gandhi Government General Hospital, Park Town, Chennai, which is a tertiary care institute.

STUDY DESIGN:

- The study was a prospective observational study.

- Consecutive immunocompromised patients who presented with pulmonary diseases were included in the study.

- No specific method of randomization was used.

- No controls were used in the study.

STUDY PERIOD:

8 months, from January 2016 – August 2016.

SUBJECT SELECTION:

A total 592 patients referred from other departments like Oncology, Nephrology, Rheumatology, Hematology from January 2016 – July 2016 above the age of 12 years to Thoracic medicine department for evaluation of pulmonary diseases were screened.
INCLUSION CRITERIA:

Among them 120 patients satisfying definition of immunosuppression with any one of the following features were evaluated,

1. Chest symptoms like cough, sputum, breathlessness, chestpain, hemoptysis with or without fever.
2. Abnormal auscultatory finding like crackles, wheeze with or without symptoms.
3. Presence of pulmonary infiltrates in radiography

Immunosuppression was defined by standard guidelines using IDSA ³ and CDC ⁴ guidelines on vaccination for immune compromised host.

DEFINITION FOR IMMUNOSUPPRESSION

1. Receiving cancer chemotherapy
2. Receiving daily corticosteroid therapy with a dose ≥20 mg of prednisone or equivalent for ≥14 days
3. Receiving certain biologic immune modulators, that is, tumor necrosis factor-alpha (TNF-α) blocker or rituximab
4. Those receiving methotrexate (MTX) ≤0. 4 mg/kg/week, azathioprine ≤3 mg/kg/day, or 6-mercaptopurine ≤1. 5 mg/kg/day
5. Solid organ transplant recipients
6. Hematological malignancies
7. Chronic kidney disease on hemodialysis
EXCLUSION CRITERIA:

Out of the 120 patients satisfying inclusion criteria 30 patients were excluded from the study based on the following reasons,

1. All HIV positive patients were excluded from the study.
2. All sputum AFB smear positive pulmonary tuberculosis were excluded from the study.
3. Patients having very poor general condition, very severe breathlessness, recent history of myocardial infarction and patients not fit for bronchoscopy.
4. Patients not willing to give informed written consent.

METHODOLOGY

➢ Bronchoscopy was planned in the remaining 90 patients and they underwent complete clinical evaluation.

Informed consent was obtained after explaining the nature of the study.

1. The following data were collected from the patient
   • Name, Age, Sex, Residential address, Occupation
2. Detailed clinical history was collected which included
   • The presenting complaints/symptoms and their duration, including presenting illness.
   • The nature of the primary disease for which patients are undergoing current treatment like, Chronic Kidney Disease, Rheumatological Diseases, Carcinoma, Hematological diseases etc.
• The past history of any similar illness or respiratory problems
• A detailed treatment history, which includes the immunosuppressive agents patients are currently receiving like corticosteroids, Biological Agents, chemotherapeutic agents etc., their dosage and duration.
• Personal history, family history and occupational history
• History of any comorbidities such as coronary artery disease, recent MI, systemic hypertension, Diabetes Mellitus etc.

3. General examination and a structured clinical examination of the respiratory system and other systems were done.

4. Basic blood investigations were done in all patients like Complete blood count, Renal function test, Bleeding time, Clotting time, Prothrombin time, Activated partial thromboplastin time.

5. Chest Skiagram anteroposterior, lateral view, routinely Plain computed tomography (CT CHEST) chest/contrast enhanced computed tomography chest (CECT-CHEST)/ High resolution computed tomography chest (HRCT-CHEST) were done as required depending on the patient's diagnosis and clinical status.

6. A careful pre-evaluation and cardiac fitness which includes an echo was done prior to Fiber optic bronchoscopy (FOB) in all patients.

➢ After complete clinical evaluation, blood investigations and pre procedure evaluation,10 patients were excluded from the study for following reasons

• Very high cardiac risk
• Coagulation abnormalities or very low platelet count < 50,000 cells/mm3
The remaining 80 patients included in study were already receiving empirical antimicrobial therapy for their abnormal symptoms, signs or radiological lesions by the treating physician. Out of which 11 patients who showed clinical improvement to the current empirical treatment as noted by the treating physician during pre-procedure evaluation were further excluded from the study.

The remaining 69 underwent bronchoscope. Bronchoscopy (FOB) was done as per British Thoracic Society guideline for diagnostic flexible bronchoscopy in adults using an Olympus fiber optic bronchoscope and strict disinfection protocol was followed for disinfecting the scope pre and post bronchoscopy as per the above mentioned guidelines.

In 4 patients bronchoscopy could not be completed due to poor patient cooperation were further excluded from the study.

**SAMPLE SIZE**

A total 65 patients FOB was completed and BAL sample was sent for analysis.

**ANALYSIS OF BAL SAMPLE**

Bronchoalveolar lavage was done from the lobe affected and segment involved and sample collected was sent for

- **GENE XPERT MTB** – A real time cartridge based nucleic acid amplification test for diagnosis of Mycobacterium Tuberculosis done at STATE INTERMEDIATE LEVEL REFERENCE
LABORATORY AND INSTITUTE OF THORACIC MEDICINE, CHETPET.

➢ AFB staining
➢ Bacterial culture and sensitivity & Grams staining
➢ Fungal culture & KOH staining
➢ Cytology

During bronchoscopy

◆ Transbronchial & Endobronchial biopsy was done as required on case to case basis provided there were no contraindications to procedure like, prolonged bleeding time, clotting time, severe hypoxemia likely to worsen during bronchoscopy, Poor general condition, unstable cardiovascular status, advanced renal failure etc ⁴⁷,⁴⁸.

TECHNIQUE OF BRONCHOALVEOLAR LAVAGE ⁴⁹

• Bronchoalveolar Lavage was done as per the standard guidelines prescribed by European Respiratory Task Force – Recommendation of standardized of BAL Technique (1999) ⁴⁹

PROCESSING OF BRONCHO ALVEOLAR LAVAGE SAMPLE

The BAL sample obtained was collected in a sterile container (sterile uricol). They were then transported as early as possible to the lab in sample carrier with ice packs. If any delay in transport they were stored immediately in the refrigerator at (2-8°C).
SAMPLE PROCESSING

The samples were immediately processed after reaching the lab using standard microbiological techniques. Routine methods like Gram’s staining and AFB (Acid Fast Bacilli) staining were done on all samples. Then they were inoculated on standard culture media for detecting bacterial growth like blood agar and Mac Conkey agar (MAC). Culture for fungi was done by using Sabouraud’s Dextrose Agar (SDA) medium. To check the presence of fastidious organisms and also to rule out the presence of anaerobic organisms special media like Thioglycollate broth (TGB) was also inoculated.

The plates and tubes were incubated at 37C in an incubator. The blood agar plates were incubated in a candle jar with 5-10% Co2. After overnight incubation, the plates and tubes were examined for presence of growth. The TGB tubes were incubated till 7 days before declaring a negative result. The SDA plates were incubated for 4 weeks to allow for the growth of slow growing fungi.

If growth was present in Blood agar (BA) and MAC plates, then the significance of the growth was assessed by doing a colony count. In a BA plate the hemolysis produced by the colonies are noted. Standardized tests like catalase and oxidase tests were performed on colonies from non-selective medium.

Identification of the bacterial species is done by using standard biochemical tests like an Indole test (using Kovac’s reagent), MMM medium (Mannitol Motility Medium), citrate test, urease test, Triple Sugar Iron medium (TSI) and sugar fermentation tests.
Identification of the fungal species is done by detecting growth in SDA plates and doing an LPCB (Lacto Phenol Cotton Blue) mount on the culture. Yeasts like Candida were identified using Gram’s staining, germ tube test and assimilation and fermentation tests. Speciation of Candida was done using a special media called CHROM agar.

**DIAGNOSTIC CRITERIA TO DETERMINE INFECTIOUS ETIOLOGY IN BAL**

1. **TUBERCULOSIS:** AFB staining positive in lavage fluid or MTB detected by CBNAAT (Real Time Cartridge Based Nucleic Acid Amplification Method)

2. **BACTERIAL INFECTIONS:** BAL fluid contains $\geq 10^4$ CFU/ml in cultures of BAL 1 ml and < 1% squamous epithelial cells in Geimsa stained smears$^{51,34}$

3. **FUNGAL INFECTIONS:** (European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group DEFINITION WAS USED)
   - 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$^{52}$
• **Criteria for proven invasive fungal disease except for endemic Mycoses**

  ❖ **Microbiological analysis:**
  
  Histopathologic, cytological or direct microscopic examination of a specimen obtained by needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage

  ❖ **Culture**
  
  Recovery of a mold or “black yeast” by culture of a specimen obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding bronchoalveolar lavage fluid, a cranial sinus cavity specimen, and urine

• **Criteria for probable invasive fungal disease except for Endemic Mycoses**

  1. **Host factors:**

     a. Recent history of neutropenia (<500 neutrophils/mm$^3$ for >10 days) temporally related to the onset of fungal disease

     b. Receipt of an allogeneic stem cell transplant

     c. Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a mean minimum dose of 0.3 mg/kg/day of prednisone equivalent for >3 weeks

     d. Treatment with other recognized T cell immunosuppressants, such as cyclosporine, TNF-α blockers, specific monoclonal
antibodies (such as alemtuzumab), or nucleoside analogues during the past 90 days

e. 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:

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

b. Air-crescent sign

c. Cavity

3. Mycological criteria:

A. DIRECT TEST (cytology, direct microscopy, or culture)

Mold in sputum, bronchoalveolar lavage fluid, bronchial brush, or sinus aspirate samples, indicated by 1 of the following:

• Presence of fungal elements indicating a mold

• Recovery by culture of a mold (e.g., Aspergillus, Fusarium, Zygomycetes, or Scedosporium species)

B. INDIRECT TESTS (detection of antigen or cell-wall constituents)

Aspergillosis

• Galactomannan antigen detected in plasma, serum, BAL fluid, or CSF

• Invasive fungal disease other than cryptococcosis and zygomycoses

• β-d-glucan detected in serum
CRITERIA FOR THE DIAGNOSIS OF ENDEMIC MYCOSES

(Endemic Mycoses includes histoplasmosis, blastomycosis, coccidioidomycosis, paracoccidioidomycosis, sporotrichosis, and infection due to Penicillium marneffei.)

PROVEN ENDEMIC MYCOSIS

In a host with an illness consistent with an endemic mycosis, 1 of the following:

a. Recovery in culture from a specimen obtained from the affected site or from blood

b. Histopathologic or direct microscopic demonstration of appropriate morphological forms with a truly distinctive appearance characteristic of dimorphic fungi, such as Coccidioides species spherules, Blastomyces dermatitidis thick-walled broad-based budding yeasts, Paracoccidioides brasiliensis multiple budding yeast cells, and, in the case of histoplasmosis, the presence of characteristic intracellular yeast forms in a phagocyte in a peripheral blood smear or in tissue macrophages

PROBABLE ENDEMIC MYCOSIS

The presence of a host factor, including but not limited to those specified plus a clinical picture consistent with endemic mycosis and Mycological evidence, such as a positive Histoplasma antigen test result from urine, blood, or CSF
TREATMENT MODIFICATION & FOLLOW UP

- Patients were allowed to continue with same empirical treatment until the results of bronchoscopy were available.
- Appropriate Treatment modification was done based on the results.
- Patients diagnosed as tuberculosis were started on Anti-Tuberculous Treatment.
- For bacterial infections antimicrobials were changed as per culture sensitivity pattern if needed.
- For fungal infections antifungals were started in patients with proven and probable invasive fungal infections.
- Patients diagnosed with malignancy and lymphoma were referred back to oncology department for restarting chemotherapeutic regimens.

Patients were followed up until the signs of clinical improvement or discharge or death in hospital. Post discharge patients were enquired for clinical improvement during their follow up visits to the hospital or through telephone calls.

DEFINITIONS

INFECTIONOUS ETIOLOGY

When microorganisms grown in culture consistent with above diagnostic criteria for bacterial or fungal infections or BAL fluid AFB smear positive or MTB detected in GeneXpert.
NON-INFECTIONOUS ETIOLOGY

No organism isolated from a bacterial/fungal culture or AFB staining negative or GeneXpert MTB not detected.

PLUS

Alternative diagnosis established by cytology positive for malignant cells or HPE proof for lymphomatous infiltration or malignancy or radiation fibrosis or DAH was diagnosed by established criteria.\textsuperscript{53,54}

POSITIVE YEILD OF FOB:

When an infectious or non-infectious cause was established by bronchoscopy.

NEGATIVE / NON-DIAGNOSTIC YEILD:

When no definitive infectious or non-infectious cause could be established by bronchoscopy.

STATISTICAL ANALYSIS:

All statistical analysis was performed using the Statistical Package for Social Science (SPSS, version 17) for Microsoft windows. Descriptive statistics were presented as numbers and percentages. A chi-square test was used for comparison between two attributes. A two-sided p value < 0.05 was considered statistically significant.
STUDY PROTOCOL

STEP 1
SUBJECT SELECTION
n = 592 (subjects referred from Nephrology, Rheumatology, Oncology, Hematology with suspected pulmonary diseases)

STEP 2
SUBJECT INCLUSION n = 120
(satisfying definition for immune suppression & with pulmonary symptoms/signs/lesion in chest radiography)

STEP 3
SUBJECT EXCLUSION
(30 patients excluded based on exclusion criteria) n = 90

STEP 4
PRE-PROCEDURE EVALUATION
(10 patients excluded due to high risk for procedure & 11 patients improved clinically hence excluded) n = 69

STEP 4
BRONCHOSCOPY DONE n= 69
(4 patients excluded as not cooperative for the procedure)
FOB completed n =65 (sample size) & BAL sent for analysis

STEP 5
TREATMENT MODIFICATION
Empirical Treatment modified based on bronchoscopic results & patients followed for clinical improvement until discharge.
RESULTS AND ANALYSIS

AGE DISTRIBUTION:

A total number of 65 patients were included in the study.

The mean age of 65 patients was 41.91 with a standard deviation of 15.5. The age of patients ranged from 15 years – 74 years. The patients were equally divided among two age groups < 40 years & > 40 years with 51% and 49% respectively.

TABLE 3: AGE DISTRIBUTION

| AGE DISTRIBUTION 41.91 +/- 15.5 | Freq | Percentage |
|---------------------------------|------|------------|
| < 40 YEARS                      | 33   | 51%        |
| > 40 YEARS                      | 32   | 49%        |
| TOTAL                           | 65   | 100%       |
FIG 1: AGE DISTRIBUTION

GENDER DISTRIBUTION:

Out of 65 patients included in study 36 were male and 29 were females. Thus, ratio was 55% & 45% male to female.

TABLE 4: GENDER DISTRIBUTION

| GENDER DISTRIBUTION | FREQ | %    |
|---------------------|------|------|
| MALE                | 36   | 55%  |
| FEMALE              | 29   | 45%  |
| TOTAL               | 65   | 100% |

FIG 2: GENDER DISTRIBUTION

N=65
DIFFERENT GROUP OF IMMUNOCOMPROMISED PATIENTS INCLUDED IN THE STUDY

The 65 patients included in the study were divided into 5 groups based on their disease pattern and nature of immunosuppression.

**GROUP 1:** Cancer patients who were receiving chemotherapy in past 6 months

**GROUP 2:** Post Renal Transplant recipients who were receiving immunosuppressants.

**GROUP 3:** Chronic Renal Failure patients currently receiving haemodialysis

**GROUP 4:** Patients with Hematological Malignancies who were immunosuppressed because of their disease per se as well as receiving chemotherapy

**GROUP 5:** Connective Tissue Disease patients like SLE, RA, etc, who were receiving steroids > 20 mg/day for more than 1 month or receiving immunosuppressive drugs or Biological agents.

| TABLE 5: DIFFERENT GROUPS OF IMMUNOCOMPROMISED PATIENTS |
|----------------------------------------------------------|
| DIFFERENT GROUPS OF IMMUNOCOMPROMISED PATIENTS            |
| FREQ | PERCENTAGE |
| CANCER CHEMOTHERAPY GROUP | 11 | 17% |
| POST RENAL TRANSPLANT GROUP | 9 | 14% |
| CHRONIC KIDNEY DISEASE GROUP | 16 | 25% |
| HAEMATOLOGICAL MALIGNANCIES | 8 | 12% |
| CONNECTIVE TISSUE DISEASES | 21 | 32% |
| TOTAL | 65 | 100% |
The presenting symptoms of the patients were

- **CHEST SYMPTOMS ALONE**: Consisted of cough with expectoration, dry cough, Dyspnea, Chest pain etc.

- **CHEST SYMPTOMS ALONG WITH FEVER**

- **FEVER ALONE**

- **HEMOPTYSIS**

- **ASYMPTOMATIC**
### TABLE 6: PRESENTING SYMPTOMS

| SYMPTOMS                        | FREQ | %  |
|---------------------------------|------|----|
| CHEST SYMPTOMS ALONE           | 36   | 55% |
| CHEST SYMPTOMS WITH FEVER      | 11   | 17% |
| HEMOPTYSIS                     | 9    | 14% |
| FEVER ALONE                    | 6    | 9%  |
| ASYMPTOMATIC                   | 3    | 5%  |
| **TOTAL**                      | **65** | **100%** |

**FIG 4: PRESENTING SYMPTOMS**
DURATION OF SYMPTOMS

Duration of symptoms was divided into 4 groups:

- **ACUTE ONSET** - < 3 weeks
- **SUBACUTE ONSET** – 3-8 weeks
- **CHRONIC** - > 8 weeks
- **ASYMPTOMATIC**

### TABLE 7: DURATION OF SYMPTOMS

| DURATION OF SYMPTOMS | FREQ | %  |
|----------------------|------|----|
| < 3 WEEKS            | 34   | 52%|
| 3-8 WEEKS            | 20   | 31%|
| > 8 WEEKS            | 8    | 12%|
| ASYMPOTOMATIC        | 3    | 5% |
| TOTAL                | 65   | 100%|

**FIG 5: DURATION OF SYMPTOMS**
RADIOLOGICAL FINDINGS

The radiological findings at the time of presentation were divided into followings groups based on the predominant pattern as assessed by the pulmonologist:

- Consolidation pattern, Ground Glass Opacities, Tree-in-Bud pattern, Cavity, Reticular & Nodular pattern.

| TABLE 8: RADIOLOGY DIFFERENT FORMS OF RADIOLOGICAL INVOLVEMENT |
|---------------------------------------------------------------|
| **FREQ** | **%** |
| CONSOLIDATION | 31 | 48% |
| GROUND GLASS OPACITIES | 9 | 14% |
| CAVITY | 7 | 11% |
| TREE IN BUD APPEARANCE | 4 | 6% |
| RETICULAR PATTERN | 8 | 12% |
| NODULAR PATTERN | 6 | 9% |
| TOTAL | 65 | 100% |

FIG 6: DIFFERENT PATTERNS OF RADIOLOGICAL INVOLVEMENT
ALVEOLAR VS NON-ALVEOLAR PATTERN

Consolidation, GGO, Cavity, Tree in Bud were considered together as alveolar pattern and Reticular & Nodular predominant forms were considered as non-alveolar pattern

TABLE 9: ALVEOLAR VS NON-ALVEOLAR PATTERN

| ALVEOLAR VS NON-ALVEOLAR PATTERN | FREQ | %    |
|----------------------------------|------|------|
| ALVEOLAR PATTERN                | 51   | 79%  |
| NON-ALVEOLAR PATTERN            | 14   | 21%  |
| TOTAL                           | 65   | 100% |

FIG 7: ALVEOLAR VS NON-ALVEOLAR PATTERN
LOBE INVOLVEMENT (CT CHEST)

In our study lobe involvement was divided into Upper Lobe, Middle Lobe/Lingula, Lower Lobe.

| LOBE INVOLVEMENT | FREQ | % |
|------------------|------|---|
| UPPER LOBE       | 21   | 32%|
| MIDDLE LOBE/LINGULA | 17   | 26%|
| LOWER LOBE       | 27   | 41%|
| TOTAL            | 65   | 100%|

FOCAL VS DIFFUSE INVOLVEMENT

Involvement of single lobe was considered as focal & involvement of 2 or more lobes was considered as diffuse.

FIG 8: FOCAL VS DIFFUSE INVOLVEMENT OF LOBES
YIELD OF BRONCHOSCOPY

In our study bronchoscopy gave positive results in 80% (52 cases) and no diagnosis could be obtained even after bronchoscopy in 20% (13 cases)

POSITIVE YIELD: Yield considered to be positive when infectious etiology like TB (diagnosed by Bronchial Wash GeneXpert/ AFB smear positivity), BACTERIAL, FUNGAL organisms were diagnosed by culture OR noninfectious causes were diagnosed by Histopathological examination & cytology.

NEGATIVE YIELD: when no diagnosis could be obtained.

FIG 9: YIELD OF BRONCHOSCOPY
INFECTIOUS VS NON-INFECTIONOUS ETIOLOGY DIAGNOSED BY BRONCHOSCOPY

Out of the 80 % (52 cases) of positive bronchoscopic yield 65% (42) were due to infectious etiology and remaining 15% (10) were due to non-infectious causes.

**TABLE 11: YIELD OF BRONCHOSCOPY**

| BRONCHOSCOPIC YEILD               | FREQ | %   |
|-----------------------------------|------|-----|
| INFECTIOUS ETIOLOGY               | 42   | 65% |
| NON-INFECTIONOUS ETIOLOGY         | 10   | 15% |
| NO DIAGNOSIS OBTAINED             | 13   | 20% |
| TOTAL                             | 65   | 100%|

**FIG 10: INFECTIOUS VS NON-INFECTIONOUS ETIOLOGY – BY BRONCHOSCOPY**
SPECTRUM OF PULMONARY INFECTIONS

Among the infectious causes of pulmonary diseases in immunocompromised patients, bacterial infections were predominant with 24%, followed by mixed infections by 15%, tuberculosis 14% & fungal 12%.

TABLE 12: SPECTRUM OF PULMONARY INFECTIONS

| ORGANISM IDENTIFIED       | FREQ | %  |
|---------------------------|------|----|
| BACTERIAL ALONE           | 15   | 24%|
| TUBERCULOSIS ALONE        | 9    | 14%|
| FUNGAL ALONE              | 8    | 12%|
| MIXED                     | 10   | 15%|
| NON-INFECTIOUS            | 10   | 15%|
| NO DIAGNOSIS              | 13   | 20%|
| TOTAL                     | 65   | 100%|

FIG 11: SPECTRUM OF PULMONARY INFECTIONS
## TYPES OF MIXED ORGANISMS IDENTIFIED

### TABLE 13: PATTERN OF MIXED ORGANISMS

| ORGANISMS                              | FREQ |
|----------------------------------------|------|
| TUBERCULOSIS + BACTERIAL               | 3    |
| TUBERCULOSIS + FUNGAL                 | 2    |
| BACTERIAL + FUNGAL                    | 4    |
| TUBERCULOSIS + BACTERIAL+ FUNGAL      | 1    |
| **TOTAL**                             | **10**|

### FIG 12: SPECTRUM OF MIXED ISOLATES

- TB + BACTERIAL
- TB+ FUNGAL
- BACTERIAL + FUNGAL
- TB+BACTERIAL+FUNGAL

**SPECTRUM OF MIXED ORGANISMS ISOLATED**
SPECTRUM OF BACTERIAL INFECTIONS

Overall out of 65 patients in the study bronchial wash bacterial culture was positive in 22 patients. In one patient two organisms were isolated. So totally 23 organisms isolated contributing to 35% of infection in immunocompromised patients.

**TABLE 14: SPECTRUM OF BACTERIAL INFECTIONS**

| BACTERIAL ISOLATES IDENTIFIED BY BAL CULTURE | FREQ | %  |
|---------------------------------------------|------|----|
| BACTERIAL ALONE                             | 15   | 23%|
| BACTERIAL + OTHER ORGANISMS (TB/ FUNGAL)    | 8    | 12%|
| NEGATIVE FOR BACTERIAL CULTURE              | 42   | 65%|
| TOTAL                                       | 65   | 100%|

**FIG 13: PROPOTION OF BACTERIAL INFECTIONS DIAGNOSED BY BAL CULTURE**
## BAL BACTERIAL CULTURE RESULTS

| BACTERIA ISOLATED                  | FREQ | %  |
|-----------------------------------|------|----|
| STREPTOCOCCUS PNEUMONIAE          | 1    | 1.5% |
| KLEBSIELLA PNEUMONIAE             | 5    | 7.5% |
| PSEUDOMONAS AERUGINOSA            | 7    | 10.5% |
| ACINETOBACTER                     | 3    | 4.5% |
| MRSA                              | 5    | 7.5% |
| ENTEROCOCCI                       | 2    | 3%  |
| E. COLI                           | 1    | 1.5% |

**FIG 14: SPECTRUM OF BACTERIAL INFECTIONS**
SPECTRUM OF FUNGAL INFECTIONS

Out of 65 patients in whom BAL was done fungal culture was positive in 15 cases, contributing to 23% of pulmonary infections. Out of 15 BAL fungal culture positive, in 8 patients, fungi were alone, isolated & in remaining 7 cases, fungi were isolated with other organisms (Bacterial/TB)

| TABLE 16: SPECTRUM OF FUNGAL INFECTIONS |
|----------------------------------------|
| FUNGAL ORGANISMS ISOLATED FROM BAL CULTURE |
| FREQ | % |
| FUNGAL ALONE ISOLATED | 8 | 12% |
| FUNGAL + OTHER ORGANISMS | 7 | 11% |
| NEGATIVE FOR FUNGAL CULTURE | 50 | 77% |
| TOTAL | 65 | 100% |

FIG 15: PROPORTION OF FUNGAL INFECTIONS IDENTIFIED BY BAL CULTURE
FUNGAL ORGANISMS GROWN IN BAL FUNGAL CULTURE

TABLE 17: FUNGAL ORGANISMS

| FUNGAL ISOLATES IN BAL | FREQ | %   |
|------------------------|------|-----|
| CANDIDA ALBICANS       | 2    | 3%  |
| CANDIDA TROPICALIS     | 1    | 1.5%|
| CANDIDA PARASILOPSIS   | 1    | 1.5%|
| PENICILLIUM MARNEFFI   | 1    | 1.5%|
| ASPERGILLUS NIGER      | 4    | 6%  |
| ASPERGILLUS FUMIGATUS  | 3    | 4.5%|
| ASPERGILLUS FLAVUS     | 2    | 3%  |
| ASPERGILLUS VERSICOLOR | 1    | 1.5%|

FIG 16: SPECTRUM OF PULMONARY INFECTIONS
PROVEN / PROBABLE FUNGAL INFECTIONS VS COLONISERS

Out of 15 cases of fungal infections diagnosed by BAL culture, Anti-Fungal drugs were started only in 9 patients. The remaining were thought to be due to colonizers in the bronchial tree.

FIG 17: SPECTRUM OF FUNGAL INFECTIONS

FIG 18: CO-INFECTIONS - FUNGAL ISOLATED AS COLONISERS AS PER DIAGNOSTIC CRITERIA
SPECTRUM OF TUBERCULOUS INFECTIONS

Out of 65 immunocompromised patients, 15 patients BAL GeneXpert MTB was detected, contributing to 24% of pulmonary infections. In 9 patients, tuberculosis alone was detected & and remaining 6 TB was detected with other organisms.

**TABLE 18: SPECTRUM OF TUBERCULOSIS**

| TUBERCULOUS INFECTION DIAGNOSED IN BAL BY GENEXPERT | FREQ | %  |
|-----------------------------------------------------|------|-----|
| TUBERCULOSIS ALONE                                  | 9    | 14% |
| TUBERCULOSIS + FUNGAL                              | 2    | 3%  |
| TUBERCULOSIS + BACTERIAL                            | 4    | 6%  |
| TUBERCULOSIS + BACTERIAL + FUNGAL                  | 1    | 1%  |
| NEGATIVE FOR TUBERCULOS                             | 50   | 76% |
| TOTAL                                               | 65   | 100 |

**FIG 18: PROPORTION OF PULMONARY TB DETECTED BY BAL**
**DRUG SENSITIVITY PATTERN AMONG TUBERCULOSIS INFECTION**

Out of 15 patients in whom Bronchial Wash GeneXpert MTB was detected 1 showed rifampicin resistant, 1 showed indeterminate pattern, remaining were rifampicin sensitive.

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**FIG 19: DRUG SENSITIVITY AMONG TUBERCULOSIS PATIENTS.**
NON-INFECTIONOUS ETIOLOGY DIAGNOSED BY BRONCHOSCOPY

TABLE 19: NON-INFECTIONOUS CAUSES

| NON-INFECTIONOUS CAUSES OF PULMONARY INFILTRATES | FREQ | %  |
|-----------------------------------------------|------|----|
| MALIGNANCY DIAGNOSED BY CYTOLOGY/ HPE          | 6    | 9% |
| HOGKINS LYMPHOMA – LYMPHOMATOUS INFILTRATION  | 1    | 1.5% |
| RADIATION FIBROSIS                              | 1    | 1.5% |
| ALVEOLAR HAEMORRHAGE                            | 1    | 1.5% |
| INTERSTITIAL FIBROSIS                           | 1    | 1.5% |
| TOTAL                                          | 10   | 15% |

FIG 20: SPECTRUM OF NON-INFECTIONOUS CAUSES OF PULMONARY DISEASES
COMPLICATIONS OF BRONCHOSCOPY

Out of 65 immunocompromised patients in whom bronchoscopy was done for evaluation of pulmonary diseases 76% did not have any complications and in remaining 24% minor complications were present.

| COMPLICATIONS OF BRONCHOSCOPY | FREQ | %  |
|-------------------------------|------|----|
| TRANSIENT HYPOXEMIA          | 10   | 15%|
| MINOR BLEEDING               | 5    | 8% |
| PNEUMOTHORAX                 | 1    | 1% |
| NO COMPLICATIONS             | 49   | 76%|
| TOTAL                        | 65   | 100%|

FIG 21: COMPLICATIONS OF BRONCHOSCOPY
CHANGE IN CURRENT EMPIRICAL TREATMENT PLAN DUE TO BRONCHOSCOPIC INTERVENTION

Out of 65 immunocompromised patients in whom FOB was done the current treatment plan was changed in 37 patients as the result of bronchoscopic intervention contributing to 57%.

FIG 22: CHANGE IN TREATMENT PLAN AS THE RESULT OF BRONCHOSCOPY

TYPE OF TREATMENT MODIFICATION

| TYPE OF TREATMENT MODIFICATION | FREQ | % | IMPROVEMENT | % |
|-------------------------------|------|---|-------------|---|
| ATT STARTED                   | 15   | 23%| 11          | 75%|
| ANTIBIOTICS                   | 8    | 12%| 7           | 90%|
| ANTIFUNGALS                   | 9    | 14%| 6           | 65%|
| CHEMOTHERAPY                  | 5    | 8% | 1           | 20%|
| NO CHANGE                     | 28   | 43%|             |    |
| TOTAL                         | 37   | 57%|             |    |
CLINICAL IMPROVEMENT AS THE RESULT OF CHANGE IN EMPIRICAL TREATMENT

Out of 37 patients in whom Bronchoscopy led to change in current treatment plan 26 patients (71%) improved clinically and remaining 11 patients (29%) 4 patients died due to other comorbidities, 4 patients lost follow up and remaining 3 did not improve.

**TABLE 22: CLINICAL IMPROVEMENT IN FOLLOW UP**

| CLINICAL IMPROVEMENT DUE TO CHANGE IN TREATMENT PLAN | FREQ | %  |
|-----------------------------------------------------|------|----|
| IMPROVED CLINICALLY                                  | 26   | 71%|
| DIED DUE TO COMORBIDITIES                           | 4    | 11%|
| LOST FOLLOW UP                                      | 4    | 11%|
| NOT IMPROVED                                        | 3    | 8% |
| TOTAL                                               | 37   | 100%|

**FIG 23: CLINICAL IMPROVEMENT IN DUE TO CHANGE IN EMPIRICAL TREATMENT**
BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES IN NON-HIV IMMUNOCOMPROMISED PATIENTS IN OUR STUDY – THE OVERALL PICTURE

FIG 24: BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES

TABLE 23: OVERALL PICTURE – BRONCHOSCOPIC EVALUATION

| BRONCHOSCOPIC EVALUATION OF PULMONARY DISEASES | FREQ | %    |
|-----------------------------------------------|------|------|
| BACTERIAL INFECTIONS ALONE                    | 15   | 23%  |
| TUBERCULOSIS ALONE                            | 9    | 14%  |
| FUNGAL ALONE                                  | 8    | 12%  |
| MIXED INFECTIONS/POLYMICROBIAL                | 10   | 15%  |
| MALIGNANCY                                    | 6    | 9%   |
| HOGKINS LYMPHOMA INFILTRATION                 | 1    | 1.5% |
| RADIATION FIBROSIS                            | 1    | 1.5% |
| ALVEOLAR HAEMORRHAGE                          | 1    | 1.5% |
| INTERSTITIAL FIBROSIS                         | 1    | 1.5% |
| NO DIAGNOSIS                                  | 13   | 20%  |
| TOTAL                                         | 65   | 100% |
### COMPARISON OF SYMPTOMS WITH YIELD ON BRONCHOSCOPY

#### TABLE 24: SYMPTOMS VS YIELD

| SYMPTOMS                  | YIELD ON BRONCHOSCOPY | TOTAL (100%) |   |
|---------------------------|-----------------------|--------------|---|
|                           | POSITIVE | NEGATIVE |              |   |
| CHEST SYMPTOMS WITH FEVER | 10 (91%)  | 1 (9%)    | 11            |   |
| CHEST SYMPTOMS ALONE      | 28 (78%)  | 8 (22%)   | 36            |   |
| HEMOPTYSIS                | 8 (89%)   | 1 (11%)   | 9             |   |
| FEVER ALONE               | 6 (100%)  | 0 (0%)    | 6             |   |
| ASYMPTOMATIC              | 0 (0%)    | 3 (100%)  | 3             |   |
| TOTAL                     | 52        | 13        | 65            |   |

P VALUE 0.004

#### FIG 25: COMPARISON OF SYMPTOMS WITH BRONCHOSCOPIC YIELD

- Fever alone as presenting symptom gave a yield of 100%, followed by chest symptoms with fever with 91%
- So the presence of fever (fever alone or chest symptoms with fever) increased yield to 95% when compared to other symptoms. In asymptomatic patients there was no yield.
Comparison of radiological presentation of bronchoscopic yield

Table 25: Radiology vs yield

| Radiological Presentation         | Yield on Bronchoscopy | Total |
|----------------------------------|-----------------------|-------|
|                                  | Positive | Negative |     |
| Consolidation                    | 27 (87%) | 4 (13%)  | 31  |
| Ground Glass Pattern             | 7 (78%)  | 2 (22%)  | 9   |
| Tree in Bud Pattern              | 3 (75%)  | 1 (25%)  | 4   |
| Cavity                           | 7 (100%) | 0 (0%)   | 7   |
| Reticular/Nodular Pattern        | 8 (57%)  | 6 (43%)  | 14  |
| **Total**                        | 52       | 13       | 65  |

**FIG 26: Radiological pattern vs yield**

- Cavity had the highest yield of 100%, followed by consolidation with 87%
- The reticular / Nodular pattern had the lowest yield of 57% out of which 55% were non-infectious and 45% were infectious. Infectious causes were due to 34% tuberculosis and 11% bacterial. Noninfectious causes were malignancy, radiation fibrosis, interstitial pneumonia etc.
COMPARISON OF LOBE INVOLVEMENT IN RADIOLOGY TO YIELD

TABLE 26: LOBE INVOLVEMENT VS YIELD

| LOBE INVOLVEMENT | YIELD ON BRONCHOSCOPY | TOTAL |
|------------------|-----------------------|-------|
|                  | POSITIVE | NEGATIVE |       |
| UPPER LOBE       | 20 (95%) | 1 (5%)    | 21    |
| MIDDLE LOBE      | 12 (70%) | 5 (30%)   | 17    |
| LOWER LOBE       | 20 (74%) | 7 (26%)   | 27    |
| TOTAL            | 52       | 13        | 65    |

FIG 27: COMPARISON OF LOBE INVOLVEMENT TO BRONCHOSCOPIC YIELD

- The upper lobe disease had a better yield of 95% compared to middle & the lower lobe involvement.

- Focal involvement (involvement of one lobe) had a higher yield of 85% when compared to Diffuse disease (2 or more lobes) with 72%
COMPARISON OF YIELD IN BRONCHOSCOPY TO TREATMENT MODIFIED

- 80% (n=52) patients had a positive yield on bronchoscopy.
- Based on bronchoscopy current treatment was modified in 57% (n=37) patients

### TABLE 27: YIELD VS TREATMENT MODIFICATION

| TREATMENT MODIFIED | YIELD ON BRONCHOSCOPY | TOTAL |
|--------------------|-----------------------|-------|
|                    | POSITIVE | NEGATIVE |     |
| YES                | 37 (57%) | 0 (0%)    | 37 (57%) |
| NO                 | 15 (23%) | 13 (20%)  | 28 (43%) |
| TOTAL              | 52 (80%) | 13 (20%)  | 65 (100%) |

**P VALUE 0.000**

- Out of 65 patients in whom FOB was done the current empirical treatment plan was changed in 37 patients (57%).
- **This was statistically significant with P value of 0.000**
ANALYSIS OF DIFFERENT SUBGROUPS OF IMMUNOCOMPROMISED PATIENTS

GROUP 1: CANCER PATIENTS RECEIVING CHEMOTHERAPY PRESENTING WITH NEW PULMONARY INFILTRATES

- This group contributes to 17% (n=11) of the total population

### TABLE 28: SPLIT UP CANCER CHEMOTHERAPY GROUP

| CANCER CHEMOTHERAPY SUBGROUPS | FREQ | %  |
|-------------------------------|------|----|
| LUNG CANCER                  | 1    | 1.5%|
| ESOPHAGEAL                   | 2    | 3%  |
| STOMACH                      | 1    | 1.5%|
| PHARYNGEAL                   | 5    | 8%  |
| BREAST                       | 2    | 3%  |

SYMPTOM ANALYSIS

- 55% of patients presented predominantly with chest symptoms
- Presence of fever was less in this group. Only 27% had fever at the time of presentation & remaining 72% was afebrile.

DURATION OF SYMPTOMS

- 18% had acute/short duration of symptoms (< 3 weeks) remaining 72% had symptoms for more than > 3 weeks. When compared to other groups cancer group had longer duration of symptoms possibly because of more non-infectious nature of pulmonary disease.
### TABLE 29: DURATION OF SYMPTOMS

| Diagnosis          | Duration of Symptoms | Total |
|--------------------|----------------------|-------|
|                    | ASYMPYOMATIC | < 3 WEEKS | 3-8 WEEKS | > 8 WEEKS |
| Cancer Group       | 0 | 2 (18%) | 4 (36%) | 5 (46%) | 100% |
| Other Groups       | 3 (5%) | 28 (59%) | 20 (30%) | 3 (6%) | 100% |
| **P Value**        | 0.001 |

### RADIOLOGICAL PRESENTATION

- 46% of patients presented with consolidation followed by nodular pattern in 36%.

### TABLE 30: RADIOLOGICAL PRESENTATION

| Diagnosis | Radiological Presentation | Total |
|-----------|---------------------------|-------|
|           | Consolidation | Cavity | Nodular | Reticular | Tree | GGO |
| Cancer    | 5 (46%) | 2 (18%) | 4 (36%) | 0 | 0 | 0 | 100% |
| Others    | 28 (48%) | 5 (9%) | 2 (4%) | 8 (15%) | 4 (7%) | 9 | 100% |
| **P Value** | 0.008 |

- Nodular involvement in this group was 36% compared to only 4% in other groups. **This was statistically significant with P value 0.008**

- Focal involvement was seen in 82% as against diffuse involvement (2 or more lobes) seen only in 18%. 

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• Middle lobe/ Lower lobe involvement was seen equally in 36% each, with Upper lobe involvement in 27%.

DIAGNOSIS OF PULMONARY INFILTRATES

In cancer only 36% of pulmonary lesions were infective remaining 64% non-infectious cause. In other groups, non-infectious cause contributed to only 6%. 

This was statistically significant with chi-square P value 0.000

![Graph showing pulmonary infiltrates in cancer group vs other groups](image)

FIG 28: PULMONARY DISEASE IN CANCER GROUP VS OTHER GROUPS

ETIOLOGICAL DIAGNOSIS OF PULMONARY DISEASES.

• Among non-infective causes 54% (n=6) were due to malignancy & 9% (n=1) was due to RADIATION FIBROSIS

• Out of infective etiology TB – 9% (n=1) BACTERIAL – 9 (n=1) & FUNGAL – 18% (n=2) (Aspergillus Niger & fumigatus)
TREATMENT MODIFICATION & CLINICAL IMPROVEMENT IN CANCER PATIENTS BASED ON BRONCHOSCOPIC RESULTS

- Based on bronchoscopic results, 55% of patients, their current treatment regimen was changed.

- 10%(1 patient) ATT was started, 20%(2 patient) Antifungals started, 27%(3 patient) in whom second line chemotherapy regimens started none improved possibly because of their advanced nature of disease.

Overall, only 36% patients clinically improved when compared to other groups with 80% clinical improvement with a change in treatment. This was statistically significant with P value 0.003. This was because of possible advanced nature of underlying malignancy at time of presentation.
TABLE 30: CLINICAL IMPROMENT CANCER VS OTHERS

| DIAGNOSIS       | CLINICAL IMPROVEMENT WITH CHANGE IN TREATMENT |   |
|-----------------|---------------------------------------------|---|
|                 | IMPROVED          | NOT IMPROVED | TOTAL |
| CANCER GROUP    | 4 (36%)           | 7 (64%)      | 11    |
| OTHERS          | 43 (80%)          | 11 (20%)     | 54    |
| P VALUE         | 0.003             |              |       |

COMPLICATIONS OF BRONCHOSCOPY

- The most common complication was moderate bleeding due to biopsies.

- Mild to moderate bleeding episodes which was controlled by wedging the bleeding site and applying pressure and instillation of cold saline.

- Minor bleeding episodes in this group is 27% compared to other groups with 4%, which is statistically significant with P value 0.031

FIG 30: COMPLICATIONS DURING FOB - CANCER GROUP VS OTHERS
GROUP 2: POST RENAL TRANSPLANT PATIENTS RECEIVING IMMUNOSUPPRESSIVE DRUGS

- This group contributing to 13.8% (n=9) of the total population

SYMPTOM ANALYSIS

- 67% patients had fever with or without chest symptoms at time of presentation compared to 20% in other groups.
- This was statistically significant with P value 0.003

FIG 31: SYMPTOM ANALYSIS – RENAL TRANSPLANT VS OTHER GROUPS

- 89% presented acutely (<3 weeks) of symptoms, only 11% had symptoms more than 3 weeks.

| TABLE 31: DURATION OF POST RENAL TRANSPLANT |
|---------------------------------------------|
| DURATION OF POST RENAL TRANSPLANTATION       | NUMBER |
| < 1 MONTH                                   | 3      |
| 1-6 MONTHS                                  | 2      |
| > 6 MONTHS                                  | 4      |
RADIOLOGICAL INVOLVEMENT

- 67% presented with a consolidation pattern followed by 22% with GGO pattern.
- 55% had predominant lower lobe disease followed by 33% with Upper lobe involvement
- 67% had focal infiltrates and remaining 33% had diffuse disease.

DIAGNOSTIC YIELD OF BRONCHOSCOPY

- Out of 9 patients, 8 had a positive yield (89%) contributing 17% of overall positive yield.

PULMONARY INFECTIONS IN POST RENAL TRANSPLANT GROUP

| ETIOLOGY OF PULMONARY INFECTIONS         | FREQ | %  |
|-----------------------------------------|------|----|
| NO DIAGNOSIS                            | 1    | 11%|
| TUBERCULOSIS                            | 1    | 11%|
| FUNGAL                                  | 1    | 11%|
| BACTERIAL                                | 4    | 45%|
| MIXED (BACTERIAL + FUNGAL)              | 2    | 22%|
| NON-INFECTIVE                           | 0    | 0% |
| TOTAL                                   | 9    | 100%|

TABLE 32: SPECTRUM OF PULMONARY INFECTIONS
ETIOLOGY OF PULMONARY INFECTIONS IN POST RENAL TRANSPLANT GROUP

TABLE 33: ORGANISMS ISOLATED

| ORGANISMS ISOLATED     | FREQUENCY |
|------------------------|-----------|
| KLEBSIELLA SP          | 1         |
| PSEUDOMONAS SP         | 2         |
| ACINETOBACTER SP       | 2         |
| MRSA                   | 1         |
| CANDIDA ALBICANS       | 1         |
| CANDIDA PARASILOPSIS   | 1         |
| ASPERGILLUS NIGER      | 1         |
| TUBERCULOSIS           | 1         |
BACTERIAL INFECTIONS IN RENAL TRANSPLANT GROUP
COMPARING WITH OTHER GROUPS

Bacterial infections were more common in this group, 67% compared to other groups.

FIG 30: BACTERIAL INFECTIONS ACROSS DIFFERENT GROUPS

SPECTRUM OF PULMONARY INFECTIONS ACCORDING TO DURATION OF POST RENAL TRANSPLANT

TABLE 34: TRANSPLANT DURATION VS PULMONARY INFECTIONS

| DURATION OF POST RENAL TRANSPLANT | NO YIELD | TB | BACTERIAL | FUNGAL | MIXED |
|-----------------------------------|----------|----|-----------|--------|-------|
| < 1 MONTH                         | 0        | 0  | 2 (67%)   | 1(33%) | 0     |
| 1-6 MONTHS                       | 1(50%)   | 0  | 1(50%)    | 0      | 0     |
| > 6 MONTHS                       | 0        | 1(25%) | 1(25%) | 0     | 2(50%) |
• Immediately POST TRANSPLANT PERIOD (< 1MONTH) bacterial infections are more predominant.

• > 6 Months after transplant or after a longer duration of immunosuppression Tuberculosis was more common in our study.

TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT BASED ON BRONCHOSCOPIC YEILD

• 66% (n=6) of patients, their current empirical treatment modality was changed based on bronchoscopic results. ATT started in 11% (n=1), antibiotics changed in 33% (n=3) antifungals started in 22% (n=2)

COMPLICATIONS OF BRONCHOSCOPY

FIG 31: COMPLICATIONS BETWEEN RENAL TRANSPLANT GROUP AND OTHERS

• Overall complications were more in the renal transplant group.

• Transient hypoxemia was frequently observed (55% vs 9% in the rest).

Statistical significance was P value 0.004
GROUP 3: CHRONIC KIDNEY DISEASE PATIENTS ON MAINTENANCE HAEMODIALYSIS

- This group contributing to 25% (n=16) of the total population studied.
- Bronchoscopic yield was obtained in 69% (n=11) contributing to the overall yield of 21%.

SYMPTOM ANALYSIS IN CKD GROUP

- 62.5% presented with chest symptoms followed by 25% with Haemoptysis.
- Presence of fever was lesser in this group similar to cancer groups
- 63% patients presented with acute symptomatology (< 3 weeks) and remaining 37% with subacute presentation (3-8 weeks).

FIG 32: PRESENTING SYMPTOMS IN CKD GROUP
RADIOLOGICAL PRESENTATION

FIG 33: RADIOLOGICAL PRESENTATION CKD GROUP

- The predominant radiological pattern was consolidation occurring in 75%, followed by GGO pattern with 19%.

COMPARISON OF ALVEOLAR PATTERN/ NON-ALVEOLAR PATTERN IN CKD VS OTHER GROUPS.

TABLE 35: RADIOLOGICAL PRESENTATION – CKD VS OTHERS

| DIAGNOSIS    | RADIOLOGICAL PRESENTATION |
|--------------|----------------------------|
|              | NON-ALVEOLAR | ALVEOLAR     |
| CKD GROUP    | 0            | 16 (100%)    | 16 (100%)    |
| OTHERS       | 14 (29%)     | 35 (71%)     | 49 (100%)    |
| TOTAL        | 14           | 35           | 65           |

P VALUE 0.016

- All patients had an alveolar pattern in radiology like when compared to 71% in other groups which was statistically significant with P value 0.016
DIAGNOSTIC YIELD IN CKD GROUP

- The diagnostic yield in this group was 69% (n=11)
- There were no non-infective causes like in the renal transplant group.

SPECTRUM OF PULMONARY INFECTIONS IN CKD PATIENTS

TABLE 36: PATTERN OF PULMONARY INFECTIONS - CKD

| Pulmonary Infections in CKD Group | Freq | %   |
|----------------------------------|------|-----|
| Tuberculosis                     | 2    | 12% |
| Bacterial                        | 3    | 19% |
| Fungal                           | 2    | 13% |
| Mixed                            | 4    | 25% |
| No Diagnosis                     | 5    | 31% |

FIG 34: PULMONARY INFECTIONS IN CKD

- Out of mixed infections 3 were due to tuberculosis. (Tuberculosis + Bacteria – 1, Tuberculosis + Fungal – 2, Bacterial + Fungal – 1)
### TABLE 37: TYPES OF MICROORGANISMS

| MICROORGANISM                  | FREQUENCY |
|-------------------------------|-----------|
| TUBERCULOSIS                  | 5         |
| KLEBSIELLA SP                 | 2         |
| PSEUDOMONAS SP                | 1         |
| ACINETOBACTER SP              | 1         |
| ENTEROCOCCI                   | 1         |
| CANDIDA TROPICALS             | 1         |
| PENICILLUM SP [ ANNEXURE 2]   | 1         |
| ASPERGILLUS NIGER             | 1         |
| ASPERGILLUS FLAVUS            | 2         |

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**TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT BASED ON BRONCHOSCOPIC YEILD**

- Empirical Treatment was modified in 56% (n=9) of patients. Anti-tuberculous therapy started in 30% (n=5), antibiotic regimen changed in 12.5% (n=2) and anti-fungal drug started in 12.5% (n=2).

- 75% (n=6) in whom empirical treatment was modified improved clinically.

**COMPLICATIONS OF BRONCHOSCOPY**

- Overall complications were seen in 37% (n=6) in this group.

- The predominant complication was transient hypoxemia, which required oxygen therapy during and after procedure in 31% (n=5).
GROUP 4: PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES

- This group contributed about 12% (n=8) of the total population.
- Bronchoscopic yield was 75% and contributing to an overall yield of 12%.

TYPES OF HAEMATOLOGICAL MALIGNANCY PATIENTS

| DIAGNOSIS                        | FREQ | %  |
|----------------------------------|------|----|
| ACUTE MYELOID LEUKEMIA           | 4    | 6% |
| HODGKINS LYMPHOMA                | 3    | 4.5%|
| NON-HODGKINS LYMPHOMA            | 1    | 1.5%|

SYMPTOM ANALYSIS

- Chest symptoms were main presenting symptoms with 50%, followed by
  25% with fever & remaining 25% were asymptomatic.
**RADIOLOGICAL PRESENTATION**

- 63% presented with an alveolar pattern (consolidation, GGO, cavity)
- Upper lobe involvement was seen in 62.5% with Middle lobe/Lingular involvement in 25% and Lower lobe involvement in 12.5%.
- Focal involvement was seen in 87.5% and Diffuse involvement 12.5%.

**FIG 36: RADIOLOGICAL PATTERNS IN HAEMATOLOGICAL MALIGNACY GROUP**

**DIAGNOSTIC YIELD**

- A positive diagnostic yield is FOB was obtained in 75% (n=6)
- 62.5% (n=5) were infectious and 12.5% (n=1) were non-infectious.
- The noninfectious case was a Lymphomatous infiltration in a patient with Hodgkin’s Lymphoma presenting with right upper lobe consolidation, which was proven by Trans Bronchial lung biopsy [refer Annexure 1]
SPECTRUM OF PULMONARY INFECTIONS

FIG 37: PULMONARY INFECTIONS IN HAEMATOLOGICAL MALIGNANCY

TABLE 39: ORGANISMS IDENTIFIED – HEMATOLOGICAL MALIGNANCY

| ORGANISMS            | FREQUENCY |
|----------------------|-----------|
| KLEBSIELLA SP        | 1         |
| ASPERGILLUS NIGER    | 1         |
| ASPERGILLUS FUMIGATUS| 1         |
| CANDIDA ALBICANS     | 1         |
| TUBERCULOSIS         | 1         |

TREATMENT MODIFICATION AND CLINICAL IMPROVEMENT
BASED ON BRONCHOSCOPIC RESULTS

- Treatment was modified in 50% (n=4) based on bronchoscopic results. ATT started in 12.5% (n=1), anti-fungal started in 25% (n=2), chemotherapy restarted in 12.5% (n=1). All patients in whom treatment was modified based improved clinically.
GROUP 5: CONNECTIVE TISSUE DISEASE (CTD) PATIENTS ON CORTICOSTEROIDS/IMMUNOSUPPRESSIVE DRUGS/BIOLOGICAL AGENTS

- This group constituted around 32% (n=21) of the total studied population.
- 71% (n=15) patients had a positive yield on bronchoscopy contributing to the overall yield of 28%.

SUBTYPES OF CONNECTIVE TISSUE DISEASE PATIENTS

![Subgroups of CTD Patients]

FIG 38: SUBGROUPS OF CONNECTIVE TISSUE DISEASE PATIENTS

TYPES OF IMMUNOSUPPRESSIVE DRUGS RECEIVED

- **CORTICOSTEROIDS:** Patients received Prednisolone at a dose of > 20 mg/day on a long term basis, at least for a period of more than 4 weeks.
- **OTHER IMMUNOSUPPRESSIVE DRUGS:** Includes patients receiving a combination of immunosuppressive drugs like weekly doses of Methotrexate/ Daily doses of Azathioprine/ Daily doses of Mycophenolate Mofetil/
Cyclophosphamide on intermittent monthly doses along with or without corticosteroids.

- **BIOLOGICAL AGENTS:** Three patients received RITUXIMAB a monoclonal antibody against anti CD 20 for treatment of Rheumatoid Arthritis.

![Pie chart showing types of immunosuppressive drugs received.](image)

**FIG 39: TYPES OF IMMUNOSUPPRESSIVE DRUGS RECEIVED**

**SYMPTOM ANALYSIS**

- Most patients presented with chest symptoms like breathlessness, dry cough, because of the predominant pulmonary interstitial lung disease.
- Presence of fever was less common in this group
- Only 19% had fever with or without chest symptoms at time of presentation as compared to 81% who did not have fever, possibly because of high level of immune suppression induced by drugs.
DURATION OF SYMPTOMS

TABLE 40: SYMPTOM DURATION - CTD

| DURATION           | PERCENTAGE |
|--------------------|------------|
| ASYMPOTOMATIC      | 5% (1)     |
| 0-3 WEEKS          | 52% (11)   |
| 3-8 WEEKS          | 33% (7)    |
| > 8 WEEKS          | 10% (2)    |

- More than 50% of patients had an acute presentation with symptoms of < 3 weeks duration. Remaining 43% had longer duration of symptoms and 5% were asymptomatic referred with lesion in chest radiography.

RADIOLOGICAL PATTERN IN CTD GROUP

- The most common radiological pattern in this group is the reticular pattern due to the presence of underlying interstitial lung disease.
FIG 41: RADIOLOGICAL PATTERNS IN CTD GROUP

TABLE 41: RADIOLOGICAL PATTERN CTD VS OTHERS

| DIAGNOSIS     | RADIOLOGICAL PATTERN |
|---------------|----------------------|
|               | CONSOLIDATION | CAVITY | GGO | NODULAR | RETICULAR | TIB |
| CTD GROUP     | 29% (6)        | 14% (3) | 14% (3) | 0% | 33% (7) | 10% |
| OTHERS GROUPS | 57%            | 10%    | 14% | 14% | 2%        | 5% |

P VALUE 0.004

LOBE INVOLVEMENT IN CTD GROUP

- Lower involvement was most common 43%, followed by upper lobe 21%,
  Middle lobe/Lingular involvement in 17%
- Focal involvement was seen in 52% and diffuse involvement in 48%.
TABLE 42: LOBE INVOLVEMENT CTD VS OTHER GROUPS

| DIAGNOSIS       | LOBE INVOLVEMENT |
|-----------------|------------------|
|                 | FOCAL | DIFFUSE |
| CTD GROUP       | 52%   | 48%     |
| OTHER GROUPS    | 81%   | 18%     |

P VALUE 0.013

- In CTD group diffuse disease is more common than other groups (48% vs 18%). This was statistically significant P value 0.013.

SPECTRUM OF PULMONARY DISEASES IN CTD GROUP

FIG 42: PULMONARY INFILTRATES IN CTD PATIENTS

TABLE 43: SPECTRUM OF PULMONARY DISEASES - CTD

| PULMONARY DISEASES               | FREQUENCY |
|----------------------------------|-----------|
| TUBERCULOSIS ALONE               | 19% (4)   |
| BACTERIAL ALONE                  | 24% (5)   |
| MIXED INFECTIONS                 | 19% (4)   |
| INTESTITIAL FIBROSIS             | 5% (1)    |
| ALVEOLAR HAEMORRHAGE             | 5% (1)    |
| NO YIELD                         | 28% (6)   |
TABLE 44: MICROORGANISMS ISOLATED AND THEIR FREQUENCY

| MICROORGANISM               | FREQUENCY |
|-----------------------------|-----------|
| PSEUDOMONAS SP              | 3         |
| MRSA                        | 3         |
| ENTEROCOCCI                 | 1         |
| E. COLI                     | 1         |
| PSEUDOMONAS + MRSA          | 1         |
| ASPERGILLUS FUMIGATUS       | 1         |
| ASPERGILLUS VERSICOLOR      | 1         |
| TUBERCULOSIS                | 7         |

COMPLICATIONS OF BRONCHOSCOPY

- 95% of patients did not have any complications.

- The only one complication was due to pneumothorax, which developed during Trans Bronchial Biopsy, which needed ICD insertion.

- Overall complications in this were less when compared to other groups.
DISCUSSION

Sixty-five Non-HIV immunocompromised patients with pulmonary diseases were studied. They were divided into 5 groups, namely Cancer chemotherapy group, Post Renal Transplant Group, Chronic Kidney Disease on Haemodialysis, hematological malignancies & Connective tissue diseases on immunosuppresants.

The main goal of our study was to evaluate the diagnostic utility of early bronchoscopy in non-HIV immunocompromised patients and the therapeutic utility in terms of treatment modification and clinical improvement as the result of bronchoscopic intervention.

This is the first kind of study done in of Non-HIV immunocompromised population at our tertiary care hospital. The purpose of doing the study was because of lack of Studies done in our Indian population on bronchoscopic evaluation of pulmonary diseases especially in Non-HIV immunocompromised patients. Studies are only available in different subgroups like hematological malignancies, CKD, renal transplant recipients etc. With better chemotherapeutic drug availability for management of malignancies, well-functioning organ transplant programs, increased use of potent immunosuppressive drugs and newer biological agents for managing connective tissue diseases, more people are made immunocompromised for therapeutic reasons for management of their primary diseases. Ultimately more and more patients are developing pulmonary diseases.
and the number of referrals are being increased to the Pulmonology department for their management.

Most of these patients are already been treated empirically with multiple potent antimicrobial drugs before being our Pulmonary medicine department. There is also increasing demand from other departments to start empirical Antituberculosis Treatment once patient does not improve with empirical antimicrobial therapy. Even some of the non-infectious causes like pulmonary edema, alveolar hemorrhage, malignancy are misdiagnosed and treated as infectious empirically. Because of this empirical treatment approach, there is increased economic burden, toxicity of antimicrobial therapy, increased incidence of multidrug resistant organisms and delay in starting proper treatment. This study highlights the role of early bronchoscopy in immunocompromised patients with pulmonary diseases that are not improving with empirical treatment with regards to its diagnostic yield, safety and change in empirical treatment. Patients were also followed up to look for clinical improvement.

**AGE DISTRIBUTION**

The mean age of the patients was 41.91 with a standard deviation of 15.5. The age of patients ranged from 15 years – 74 years. The patients were equally divided among two age groups < 40 years & > 40 years with 51% and 49% respectively. The bronchoscopic yield was almost similar in both age groups with 81% in < 40 years and 78% in > 40 years. There was no statistical difference in yield, symptomatology, radiology or infections in both groups.
GENDER DISTRIBUTION

Out of 65 patients included in study 36 were male and 29 were females. Thus, ratio was 55% & 45% male to female.

SYMPTOMATOLOGY

Chest symptoms alone were the most common presentation with 55%, followed by chest symptoms along with fever in 17%. 5% of patients were asymptomatic. Presence of fever gave a higher overall yield of 95%. In asymptomatic patients, yield was zero. The statistical significance in chi-square P value was 0.004.

Kyle R. Brownback et al., 55 observed similar finding where the diagnostic yield was significantly improved in the presence of fever.

DURATION OF SYMPTOMS

52% of patients presented with acute symptoms < 3 weeks, followed by 31% with symptoms 3-8 weeks duration and 12% with > 8 weeks duration. 5% were asymptomatic. Cancer chemotherapy group had longer duration of symptoms (72% with symptoms > 3 weeks duration) at the time of presentation. Post renal transplant (89%) & CKD patients (69%) more often had shorter duration of symptoms (< 3 weeks). The statistical significance was P value < 0.05. The reason for more acute presentation in renal transplant and CKD group is because the pulmonary diseases were more of infectious etiology especially bacterial. In cancer group the disease process was mainly malignant infiltration hence fever was absent and they presented more gradually.
RADIOLOGICAL PATTERNS

Consolidation was the predominant pattern seen in 48%, followed by GGO with 14%, reticular pattern 12%, cavity 11%, nodular 9% and tree in bud 6%. Cavitary disease had a maximum yield of 100%, followed by consolidation with 87%. Reticular pattern had the lowest yield of 57%. Yield was better in an alveolar pattern of involvement in radiography.

Kyle R. Brownback et al., 55 & Danes et al 33., in their study also had similar findings, unilateral & alveolar pattern in radiography had a better diagnostic yield.

LOBE INVOLVEMENT

Lower lobe involvement was most common with 41% followed by upper lobe with 32% and middle lobe/lingula with 26%. Focal involvement (single lobe) was more common with 78%. Yield was better in upper lobe involvement & focal involvement with 95% & 85% respectively.

YIELD OF BRONCHOSCOPY

The overall yield of bronchoscopy in our study was 80% with no diagnosis obtained in remaining 20%. 65% were due to infectious causes and 15% were due to non-infectious etiology. Similar studies done in immunocompromised patients have shown wide variations in overall yield ranging from 50-80%. But in most of the studies yield has been high for an infectious etiology ranging from 60-80% similar to our study. 33,34,56,57
In a similar study done by Jain, P et al.,\textsuperscript{58} in 104 Non-HIV immunocompromised patients, the overall yield was 56.2% with high yield for an infectious etiology with 81%.

A similar study done in the Indian population of Menon LR, et al.,\textsuperscript{59}. He studied 16 renal transplants, 14 dialysis, 8 HIV positive patients, and the clinical utility of BAL in diagnosis of pulmonary infections. The overall yield was 76% of all the three groups put together. BAL cytology had a better yield when compared to culture.

**SPECTRUM OF PULMONARY INFECTIONS**

Our study results showed that in our tertiary care hospital among the immunocompromised patients bacterial infections were the predominant cause of pulmonary infections (35% overall, 23% by bacterial alone and 12% of bacterial + other organisms). Among the bacterial isolates Pseudomonas was the most common, followed by equally by Klebsiella and MRSA. This pattern is similar to the microbiological spectrum of Hospital acquired pneumonia where Gram negative organisms and MRSA are more common. These results are in accordance with several other published studies.\textsuperscript{15,8} A similar study done by Rano et al\textsuperscript{8}, showed the same results as our study. He observed in his study bacterial infections caused by MRSA and gram negative bacilli especially Pseudomonas were the most common cause of pulmonary infections. Since bacteria represent the most prevalent threat to immunocompromised patients, each institution should define the empirical antibiotic treatment based on its own data.
Tuberculosis was the second most common infectious cause (24% overall, TB alone 14% and TB + Others organisms 10%). In spite of excluding sputum AFB positive cases from the study, still the incidence of tuberculosis is quite high in our study. This highlights the importance of thoroughly searching for pulmonary tuberculosis among non-HIV immune compromised patients with pulmonary disease in high prevalence countries even if the sputum AFB smear is negative.

Jane C. Chan et al., in his study conducted in Hong Kong among 62 non-HIV immunocompromised patients found a similar result with tuberculosis being the second most common infection with a 19% incidence.

When compared with CBNAAT (gene Xpert) BAL AFB staining was able to detect only 53% of smear negative pulmonary tuberculosis cases in our study. Moreover, CBNAAT gives the added advantage of detecting Rifampicin resistance and the results are available within a few hours when compared to conventional culture which takes 8-12 weeks. Hence CBNAAT should be offered upfront to all non-HIV immunocompromised patients with pulmonary disease for diagnosis of pulmonary tuberculosis. In our study only 6% case of pulmonary tuberculosis was Rifampicin resistant, 7% showed indeterminate resistance and remaining 87% cases were rifampicin sensitive.

BAL fungal culture was positive in 23% (15 cases) in our study. But among fungal culture positive cases only 60% (9 cases) were diagnosed as proven or possible fungal infections requiring antifungal treatment as per the EORTC diagnostic criteria. In remaining 40% (6 cases) the isolated fungi from BAL culture could not be attributed to causing pulmonary disease as per diagnostic
criteria. These fungi might have colonized in the tracheobronchial tree without producing pulmonary lesions.

Among 6 patients in whom fungi were considered as colonizers 3 patients had co-infection with tuberculosis and one patient with bacteria for which they received treatment. In remaining 2 patients no other co-infection could be identified. From a CKD patient Candida tropicalis was isolated in culture and Candida albicans was isolated in BAL in AML patient. The significance of these colonizers fungi is not fully understood. Some studies have shown poor clinical outcomes in respiratory tract Candida colonization and is independently associated with increased hospital mortality\textsuperscript{22,23}.

Aspergillus species was the most common fungi isolated from respiratory tract of non-HIV immunocompromised patients in our study. Among Aspergillus species Niger was the most common, followed by Fumigatus.

Similar studies\textsuperscript{15,8,33} done in Non HIV immunocompromised patients show that among fungal infections Aspergillus is most common similar to our study.

Bacterial infections were more common among Renal Transplant Recipients (67%) & Fungal infections were more common among hematological malignancy (38%) patients and Tuberculosis was more common among CTD (38%) patients followed by CKD (31%) group.
NON-INFECTIONOUS CAUSES OF PULMONARY INFILTRATES

In our study, 15% of pulmonary infiltrates were due to non-infectious causes. Among them most common cause (9%) was malignancy diagnosed by cytology or endobronchial biopsy and the remaining (6%) were due to radiation fibrosis, alveolar hemorrhage, interstitial pneumonia & lymphomatous infiltration of the lung in a case of secondary pulmonary lymphoma.

COMPLICATIONS OF BRONCHOSCOPY

Complications of bronchoscopy in our study were only minor except one case of pneumothorax which required ICD insertion. The overall complication rate was 24%. Transient hypoxemia during and within the first hour of bronchoscopy, which required supplemental oxygen occurred in 15%, followed by mild to moderate bleeding episodes during biopsy procedures occurred in 8%. Bleeding controlled by wedging the bronchoscope at the site of bleeding and cold saline instillation. Pneumothorax occurred in 1%.

Similar studies have shown the complication rate among non-HIV immunocompromised patients ranging from 13%-21%. But complications were only minor in our study. But overall the complication rate of bronchoscopy is higher in immunocompromised patients. In general population, studies have shown the complication rate ranging widely from 5%-32%, with serious complication in 1.1% and mortality of 0.02%. There was no procedure related mortality in our study. Hence the proper pre procedural evaluation, patient selection and monitoring & care during/post procedure is necessary.
TREATMENT MODIFICATION & CLINICAL IMPROVEMENT

In our study empirical treatment was modified to the most appropriate treatment in 57% of patients based on bronchoscopic results which was statistically significant with P value 0.000. Studies have shown similar results like our study where treatment modification based on bronchoscopic yield has ranged from 38%-51%. The treatment modification rate was higher in our study compared to other studies.

Among patients in whom treatment was modified, those in whom antibiotic were changed as per culture sensitivity pattern showed maximum clinical improvement with 90%, followed by those in whom anti tuberculosis treatment was started showed 70% improvement and those in whom antifungals were started 60% clinical improvement. Those patients in whom malignancy was diagnosed and second line chemotherapeutic agents restarted only 20% showed clinical improvement probably because of their advanced nature of the disease. The overall clinical improvement with treatment modification was around 70%.

SALIENT POINTS OBSERVED AMONG CANCER CHEMOTHERAPY PATIENTS IN OUR STUDY

- Pulmonary disease in this group was more commonly due to non-infectious etiology that is malignancy.
- Because of their non-infectious nature presence of fever at the time of presentation was lower, most patients had longer duration of symptoms.
- The nodular pattern was a most common radiological pattern.
• The clinical improvement with treatment modification was low.
• Bleeding was the most common complication which could be explained because of increased endobronchial biopsy done to achieve a diagnosis

SALIENT POINTS IN POSTRENAAL TRANSPLANT GROUP IN OUR STUDY

• Fever was the predominant presenting symptom, most patients had acute symptoms at time of presentation
• Overall Bacterial infections were more common
• Immediate post-transplant period, bacterial infections were more, TB & fungal infections were more common after prolonged immunosuppression > 6 months
• Overall clinical improvement with change in treatment is good
• Transient hypoxemia during bronchoscopy was frequently encountered

SALIENT FINDINGS IN CKD GROUP

• Chest symptoms and hemoptysis are more common. Presence of fever is less in this group
• Most patients had acute presentation.
• Consolidation was a predominant radiological pattern
• Tuberculosis & bacterial infections are equally common.
• 75% of patients in whom treatment modified improved.
• Like post-transplant group hypoxemia was frequently encountered complication during the procedure
SALIENT FEATURES OF HAEMATOLOGICAL MALIGNANCY GROUP

- Chest symptoms followed by fever are most common presenting symptoms.
- Fungal infections are more predominant in this group.
- 50% of patients, treatment was modified based on bronchoscopic results and all patients in whom treatment modified improved.
- The overall complication rate is low if patients are properly worked up before the procedure like BT, CT, PT, a PTT, Platelet counts etc.

SALIENT FEATURES OF CTD GROUP

- Presence of fever at the time of initial presentation was less. This was probably because of the high level of immune suppression induced by drugs.
- In radiology reticular pattern was the most common presentation & because of the presence of underlying pulmonary interstitial involvement due to primary disease process per se.
- Diffuse pattern in radiological presentation was more common.
- Bacterial infection followed by tuberculosis were the common infective aetiologies.
- Out of 3 patients who were started on biological agents 2 developed tuberculosis.
- Bronchoscopy led to change in current treatment plan in 57%, out of which 75% improved clinically.
- Complications were low, bronchoscopy was safe and well tolerated.
CONCLUSION

➢ In our study, among Non-HIV immunocompromised patients with pulmonary diseases, we found Bronchoscopy as an useful tool. The yield of bronchoscopy was high (80%) despite empirical antimicrobial therapy.

➢ Out of positive bronchoscopic yield, 65% were due to infectious cause and 15% had non-infectious etiology. If bronchoscopy had not been performed, non-infectious cause could have been easily missed and treated as infectious.

➢ Among the infectious causes bacterial infections were the predominant cause of pulmonary disease (35% overall). Gram negative bacteria followed by MRSA were most common among the bacterial infections.

➢ Since Tuberculosis was second most common infectious cause (24% overall) it has to be ruled out in all non-HIV immunocompromised patients with pulmonary diseases in high prevalence countries.

➢ CBNAAT led to increased detection of tuberculous infection in our study when compared to BAL AFB staining. Hence genotypic test should be offered to all non-HIV immunocompromised for diagnosis of tuberculosis.

➢ Even though fungal infections were common among immunocompromised (23 % overall), we could attribute only 2/3rd as proven or probable fungal infections and remaining 1/3rd were colonizers.

➢ Presence of fever, alveolar & a focal pattern of infiltrates, upper lobe involvement increased the infectious yield of bronchoscopy.
Overall bacterial infections were more common among renal transplant group, fungal infections among hematological malignancy group and tuberculosis was more common connective tissue group followed by CKD group.

Complications of bronchoscopy in our study were only minor. Proper pre-procedure evaluation and patient selection and monitoring during the procedure reduced the complication rate.

The current empirical treatment was modified to the most appropriate treatment in 57% who underwent bronchoscopy. Among the treatment modified group, 70% improved clinically.

For clinically stable patients early bronchoscopy before starting empirical treatment can be the preferred approach. Patients who are clinically unstable or not fit for procedure, early empirical treatment is advised, followed by bronchoscopy once the general conditions improve or if the patient does not respond to empirical therapy.

In summary, bronchoscopy among Non-HIV immune compromised patients was a safe procedure with good diagnostic yield and therapeutic utility. Hence, when encountered with a non-HIV immune compromised patient with pulmonary disease, early bronchoscopy must be preferred, as the benefits outweighs the risk.
LIMITATIONS

- The sample size of the study was small, and the sample size was not distributed equally among all groups.

- Methods to detect respiratory viruses and certain atypical microbes like Mycoplasma from BAL sample was included in the study methodology.

- Since sputum AFB positive cases were excluded from the study the overall incidence of tuberculosis may be underestimated in Non-HIV immunocompromised patients.

- Very sick patients and patients with an unstable general condition were excluded from the study.

- This study was done at a specialized tertiary care hospital and hence may not reflect the pattern of infection among non-HIV immunocompromised patients at community level. So further large scale studies are needed among non-HIV immunocompromised patients.
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ANNEXURES – 1

A CASE OF RIGHT UPPER LOBE CONSOLIDATION IN A PATIENT WITH HODGKIN'S LYMPHOMA ON CHEMOTHERAPY – FOB PROVED IT AS NON-INFECTIVE CONSOLIDATION

A) CT-CHEST SHOWING RIGHT UPPER LOBE CONSOLIDATION WITH AIR BRONCHOCGRAM SIGN.

B) REED STERNBERG CELLS IN BRONCHIAL WASH

C) IHC MARKERS FROM TBLB SHOWING CD 30 & CD 15 POSITIVITY
A RARE CASE OF INVASIVE PENICILLUM MARNEFFI INFECTION IN CKD PATIENT SUSPECTED TO HAVE TUBERCULOSIS

A) SDA SLANT SHOWING PENICILLUM COLONIES

B) SDA PLATE SHOWING PENICILLUM COLONIES IN BLOOD CULTURE

C) GRAMS STAIN SHOWING EARLY CONIDIA

D) LACTO PHENOL COTTON BLUE SHOWING CONIDIA.
ABBREVIATIONS

HIV – HUMAN IMMUNODEFICIENCY VIRUS

BMT – BONE MARROW TRANSPLANT

SOT – SOLID ORGAN TRANSPLANT

BAL – BRONCHO ALVEOLAR LAVAGE

CDC – CENTER FOR DISEASE CONTROL

IDSA – INFECTIOUS DISEASE OF AMERICA

HSCT – HAEMATOPOIETIC STEM CELL TRANSPLANT

CMV – CYTOMEGALO VIRUS

RSV – RESPIRATORY SYNCYTIAL VIRUS

CLL – CHRONIC LYMPHOCYTIC LEUKEMIA

PCP – PNEUMOCYTIS CARINI PNEUMONIA

MTB – MYCOBACTERIUM TUBERCULOSIS

DAH – DIFFUSE ALVEOLAR HAEMORRHAGE

DAD – DIFFUSE ALVEOLAR DAMAGE

PBS – PROTECTED BRUSH SAMPLING

TBLB – TRANS BRONCHIAL BIOPSY
FOB – FIBER OPTIC BRONCHOSCOPY

GGO – GROUND GLASS OPACITY

BT – BLEEDING TIME, CT – CLOTTING TIME

PT – PROTHROMBIN TIME, APTT- ACTIVATED PARTIAL THROMBOPLASTIN TIME

EORTC - EUROPEAN ORGANIZATION FOR RESEARCH AND TREATMENT OF CANCER/INVASIVE FUNGAL INFECTIONS COOPERATIVE GROUP

ICD – INTER COSTAL DRAIN

CKD – CHRONIC KIDNEY DISEASE

CTD – CONNECTIVE TISSUE DISEASE

MRSA – METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS

TGB – THIOGLYCOLATE BROTH

SDA – SABURODS DEXTROSE AGAR

BA – BLOOD AGAR
"ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON-HIV IMMUNE COMPROMISED HOST"
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"ROLE OF BRONCHOSCOPY IN DIAGNOSIS OF THE PRIMARY INFECTION IN COVID-19 PATIENT"

Dedicated to the Diabetic Patients and their families by the

Department of Medicine, N.I.M.D.

The Tamil Nadu Dr. M.R. Medical University

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ETHICAL COMMITTEE APPROVAL ORDER

MADRAS MEDICAL COLLEGE, CHENNAI 600 003

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CERTIFICATE OF APPROVAL

To,
Dr. C. Palaniappan
PG in M.D.(TB & CD)
Madras Medical College/RGGH
Chennai 600 003

Dear Dr. C. Palaniappan,

The Institutional Ethics Committee has considered your request and approved your study titled “ROLE OF FIBRE OPTIC BRONCHOSCOPY IN DIAGNOSIS OF PULMONARY INFECTIONS IN NON HIV IMMUNE COMPROMISED HOST” - NO.10012016.

The following members of Ethics Committee were present in the meeting held on 12.01.2016 conducted at Madras Medical College, Chennai:

1. Dr. C. Rajendran, MD.: Chairperson
2. Dr. R. Vimala, MD., Dean, MMC, Ch-3: Deputy Chairperson
3. Prof. Sudha Seetharaman, MD., Vice Principal, MMC, Ch-3: Member Secretary
4. Prof. B. Vasanthi, MD., Inst. of Pharmacology, MMC, Ch-3: Member
5. Prof. P. Raghunath, MS, Dept. of Surgery, RGGH, Ch-3: Member
6. Prof. M. Sarath, MD., Director, Inst. of Path, MMC, Ch-3: Member
7. Tmt. J. Rajalakshmi, JAO, MMC, Ch-3: Lay Person
8. Tmt. S. Govindarajan, BA., BL., High Court, Chennai: Lawyer
9. Tmt. Arnold Sain, MA., MSW., : Social Scientist

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

21 JAN 2016

[Signature]
MEMBER SECRETARY
TAMIL CONSENT FORM

อัปปங்க்கி கட்டளை காரம்

என்று கூறும்

என்று கூறும் நான் அவ்வப் பொழுது மன்னர்களை எடுத்துணரக்கும் விளக்கம் உண்டு என்று தெரிக்கும் காரணம் காரணத்தில் உறுதியாக பதிவு செய்யப்பட்டிருக்கும்.

அவ்வாறு காண உட்பட என்று கூறும் நான் அவ்வப் பொழுது மன்னர்களை எடுத்துணரக்கும் விளக்கம் உண்டு என்று தெரிக்கும் காரணம் காரணத்தில் உறுதியாக பதிவு செய்யப்பட்டிருக்கும்.

திறன் வழக்கம் உறுதியாக கூறும் நான் அவ்வப் பொழுது மன்னர்களை எடுத்துணரக்கும் விளக்கம் உண்டு என்று தெரிக்கும் காரணம் காரணத்தில் உறுதியாக பதிவு செய்யப்பட்டிருக்கும்.

அப்படி கூறும்

என்று கூறும் நான் அவ்வப் பொழுது மன்னர்களை எடுத்துணரக்கும் விளக்கம் உண்டு என்று தெரிக்கும் காரணம் காரணத்தில் உறுதியாக பதிவு செய்யப்பட்டிருக்கும். என்று கூறும் நான் அவ்வப் பொழுது மன்னர்களை எடுத்துணரக்கும் விளக்கம் உண்டு என்று தெரிக்கும் காரணம் காரணத்தில் உறுதியாக பதிவு செய்யப்பட்டிருக்கும்.
குறுகிய என்றால் பொருள்களின் நதிக்கோட்டை அகராதி வருவதற்கு காரணம் என்றால் மதுராவின் கால குழுவத்தின் பஞ்சாதாரை எடுத்துக் கொண்டு பொருள்களை மறைந்து வெளியிட வேண்டும். ஐரோப்பிய குழுக்கள் குழுவிடம்.

இந்த பாநிக்கோட்டையில் குழுக்களை அடுக்கும் தலைமுகத்தை அருகில் கொண்டு வரும்போது காலமாக பயிரை அளிக்கும் வழியாக கொண்டு வரும்.

இந்த குழுக்களின் முழுதும் வருகையை மாற்றாக பொருள்களை நழுவூடு வழிகாட்டுக்கோட்டை வளர்ந்து வைக்கவேண்டும். இந்த குழுக்களின் முழுதும் வருகையை மாற்றாக பொருள்களை நழுவூடு வழிகாட்டுக்கோட்டை வளர்ந்து வைக்கவேண்டும்.

அருங்காட்சியில் நிறம் பல்கரையில் நிறம்

அருங்காட்சியில் கோணாம்பின் பல்கரையில்
PATIENT CONSENT FORM

Study Detail: Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.

Study Centre: Rajiv Gandhi Government General Hospital, Chennai.

Patient’s Name:
Patient’s Age:
Identification Number:

Patient may check (✓) these boxes:

a) I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

b) I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

c) I understand that sponsor of the clinical study, others working on the sponsor’s behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

d) I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or wellbeing or any unexpected or unusual symptoms.

e) I hereby consent to participate in this study.

f) I hereby give permission to undergo detailed clinical examination, Radiographs, blood investigations and surgical procedure as required.

Signature/thumb impression ___________________________ Signature of Investigator ___________________________

Patient name and address ___________________________ Study investigators name: ___________________________

[DR C. PALANIAPPAN]
PATIENT INFORMATION SHEET

TITLE OF THE STUDY: Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.

We are conducting a study on among patients admitted in Rajiv Gandhi Government General Hospital, Chennai

The purpose of this study is to analyse The Role of Bronchoscopy in diagnosis of pulmonary infiltrates in non HIV immune compromised host.

We are selecting cases of immunocompromised patients who are HIV negative with persistent lung infiltrates in radiography despite antibiotic therapy as per the definition and the selected

Patients will undergo basic blood investigations, CT chest (if needed), fibre-optic bronchoscopy and CT guided Biopsy (if necessary) to arrive at a diagnosis and subsequently treat the patient.

The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled.

The results of the special study may be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

Signature of investigator: ____________________________  Signature of participant: ____________________________

Date: ____________________________
EVALUATION FORM

Name:
Age:
Sex:
IP number:
Ward:
Presenting complaints:
History of presenting illness:
Past history:
Treatment history:
Personal history:
Occupational history:
General examination:
Systemic examination:
Blood investigations:
Radiological findings:
Chest x-ray:
CT-CHEST:
Sputum investigations:
Bronchoscopy findings and investigation results:
Transbronchial/Endobronchial biopsy reports:
Final diagnosis:
# MASTER CHART

| S No | Name         | Age | Sex | Diagnosis: CA (renal transplant=1) | CA Types: LEV=1 | SLE=1 | Malignancy: MEL=1 | AML=1 |
|------|--------------|-----|-----|-------------------------------------|-----------------|-------|-------------------|-------|
| 1    | S. R. Ali    | 59  | M   | 1                                   | 1               | 0     | 0                 | 0     |
| 2    | Cheenulelenu  | 80  | M   | 2                                   | 0               | 0     | 0                 | 0     |
| 3    | Ramnath     | 50  | F   | 3                                   | 0               | 1     | 0                 | 0     |
| 4    | Ravindra    | 50  | M   | 2                                   | 0               | 0     | 0                 | 0     |
| 5    | Choudharyan  | 50  | F   | 2                                   | 0               | 0     | 0                 | 0     |
| 6    | Devanathur   | 50  | M   | 0                                   | 0               | 0     | 0                 | 0     |
| 7    | Pramod      | 50  | M   | 0                                   | 0               | 0     | 0                 | 0     |
| 8    | Kumar        | 40  | M   | 1                                   | 2               | 0     | 0                 | 0     |
| 9    | Velavutha    | 85  | M   | 1                                   | 2               | 0     | 0                 | 0     |
| 10   | Subha       | 80  | F   | 1                                   | 1               | 0     | 0                 | 0     |
| 11   | Ratna       | 50  | F   | 3                                   | 0               | 0     | 0                 | 0     |
| 12   | Surendran    | 50  | M   | 3                                   | 0               | 0     | 0                 | 0     |
| 13   | Sharmila     | 40  | M   | 2                                   | 0               | 0     | 0                 | 0     |
| 14   | Samy        | 23  | F   | 1                                   | 0               | 0     | 0                 | 0     |
| 15   | Mahalakshmi  | 50  | M   | 0                                   | 0               | 0     | 0                 | 0     |
| 16   | Chandras  | 35  | M   | 4                                   | 0               | 0     | 0                 | 1     |
| 17   | Judev       | 40  | M   | 1                                   | 4               | 0     | 0                 | 0     |
| 18   | Meenakshi   | 40  | M   | 4                                   | 0               | 0     | 0                 | 2     |
| 19   | Ramnath     | 50  | M   | 5                                   | 0               | 0     | 0                 | 0     |
| 20   | Rishikul    | 50  | M   | 4                                   | 0               | 0     | 0                 | 1     |
| 21   | Pothi       | 65  | M   | 3                                   | 0               | 0     | 1                 | 0     |
| 22   | Reyadhiraun  | 87  | M   | 4                                   | 0               | 0     | 0                 | 3     |
| 23   | Uma         | 53  | F   | 5                                   | 0               | 0     | 0                 | 0     |
| 24   | Shashi      | 85  | F   | 2                                   | 0               | 1     | 0                 | 0     |
| 25   | Vighnavati   | 85  | F   | 1                                   | 0               | 0     | 0                 | 0     |
| 26   | Loyalkhan    | 27  | M   | 2                                   | 0               | 0     | 0                 | 0     |
| 27   | Nalini       | 55  | F   | 3                                   | 0               | 0     | 1                 | 0     |
| 28   | Kumbir      | 57  | M   | 1                                   | 4               | 0     | 0                 | 0     |
| 29   | Dalani      | 85  | M   | 3                                   | 0               | 0     | 0                 | 0     |
| 30   | Desigoyal   | 85  | F   | 2                                   | 0               | 0     | 0                 | 0     |
| 31   | Santida     | 23  | F   | 2                                   | 0               | 0     | 0                 | 0     |
| 32   | Attaradhi   | 85  | F   | 1                                   | 0               | 0     | 0                 | 0     |
| S.NO | NAME   | AGE | SEX | CA RETINAL TRANSPLANT | CA LUNG | CA THYROID | CA ESOPHAGUS | CA PHARYNX | CA BREAST | AUTO IMMUNE DISEASES | ECL| ELC | AML | ALL | HAEMATOLOGICAL MALIG | MCL | NHL | AML |
|------|--------|-----|-----|-----------------------|---------|------------|--------------|------------|-----------|---------------------|----|----|-----|-----|---------------------|-----|-----|-----|
| 34   | SETHA  | 31  | F   | 3                     | 0       | 0          | 0            | 0          | 3         | 0                   |    |    |     |     |                     |     |     |     |
| 35   | KARTHIKEYAN | 39 | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 36   | DEPA   | 37  | F   | 3                     | 0       | 0          | 0            | 0          | 3         | 0                   |    |    |     |     |                     |     |     |     |
| 37   | KERNAGORNTY | 35 | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 38   | CHERA  | 33  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 39   | PARTASARIY   | 37 | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 40   | GAIKMISHAER | 42 | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 41   | ANNIGRAJ | 41  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 42   | YUMILA  | 35  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 43   | LEEJA  | 32  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 44   | RAJENDRA | 56  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 45   | AKSHATA | 30  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 46   | RAJEE | 38   | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 47   | PERIMAL | 34  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 48   | LATANA | 40  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 49   | DAIL   | 33  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 50   | MURUPAS | 39  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 51   | MURUGAN | 30  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 52   | DRASAPAL | 42  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 53   | VERITA | 33  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 54   | PUNNADASI | 38  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 55   | VADURAYAN | 45  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 56   | CHANDRA | 55  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 57   | VEEL   | 20  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 58   | KENKA  | 25  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 59   | MALA   | 42  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 60   | RUMALAI | 45  | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 61   | TANALI | 35  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 62   | HETHYTHI | 48  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 63   | KALAVATHY | 50  | F   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 64   | MENAH | 25   | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| 65   | RAJEEH | 25   | M   | 3                     | 0       | 0          | 0            | 0          | 0         | 0                   |    |    |     |     |                     |     |     |     |
| S NO | NAME     | IMMUNOSUPPRESSION | CHEMOTHERAPY 1 | RENAL TRANSPLANT | SYMPTOMS CHEST SYMPTOMS | SYMPTOMS CHEST SYMPTOMS | DURATION | RADIOLGY CONSOL | CONSOL | CAVITY |
|------|----------|-------------------|----------------|------------------|-------------------------|-------------------------|----------|----------------|--------|--------|
| 1    | Jayapalan| 1                 | 0              | 0                | 3                       | 1                       | 1        |                 |        | 1      |
| 2    | Chellamuthu| 2                | 3              | 1                | 1                       | 1                       | 1        |                 | 1      | 1      |
| 3    | Rajath   | 3                 | 0              | 2                | 1                       | 1                       | 3        |                 | 1      | 1      |
| 4    | Ravendaran| 5                | 0              | 2                | 1                       | 1                       | 1        |                 | 1      | 1      |
| 5    | Chandrahanna| 2           | 3              | 1                | 1                       | 1                       | 2        |                 | 2      |        |
| 6    | Gnanasekar| 5                | 0              | 1                | 2                       | 2                       | 2        |                 |        |        |
| 7    | Prakash   | 2                 | 1              | 1                | 3                       |                          | 3        |                 |        |        |
| 8    | Imar     | 1                 | 0              | 2                | 2                       | 2                       | 4        |                 |        |        |
| 9    | Veluvinem| 1                 | 0              | 3                | 3                       | 3                       | 1        |                 |        |        |
| 10   | Sridanta | 1                 | 2              | 3                | 3                       | 3                       | 1        |                 |        |        |
| 11   | Patkayama| 2                 | 0              | 2                | 1                       | 1                       | 5        |                 |        |        |
| 12   | Sivakumar| 2                 | 3              | 1                | 1                       | 1                       | 1        |                 |        |        |
| 13   | Anandhan | 5                 | 3              | 2                | 1                       | 1                       | 1        |                 |        |        |
| 14   | Madhuran | 5                 | 0              | 2                | 1                       | 1                       | 1        |                 |        |        |
| 15   | Sathiya  | 3                 | 0              | 1                | 1                       | 1                       | 5        |                 |        |        |
| 16   | Madhanan | 1                 | 0              | 5                | 0                       | 5                       | 5        |                 |        |        |
| 17   | Chandrahar| 1                | 2              | 2                | 2                       | 2                       | 1        |                 |        |        |
| 18   | Rajendaran| 1                | 0              | 2                | 2                       | 2                       | 4        |                 |        |        |
| 19   | Methal Jayaraj| 1       | 0              | 2                | 2                       | 2                       | 4        |                 |        |        |
| 20   | Ramesh   | 2                 | 1              | 2                | 1                       | 1                       | 1        |                 |        |        |
| 21   | Rajel    | 6                 | 2              | 2                | 2                       | 2                       | 1        |                 |        |        |
| 22   | Pooja    | 2                 | 0              | 1                | 2                       | 1                       | 1        |                 |        |        |
| 23   | Jeyacharar| 6                | 0              | 2                | 1                       | 1                       | 1        |                 |        |        |
| 24   | Uma      | 4                 | 0              | 2                | 2                       | 2                       | 6        |                 |        |        |
| 25   | Shanthi  | 3                 | 0              | 2                | 1                       | 1                       | 3        |                 |        |        |
| 26   | Venkataraman| 4                | 0              | 4                | 1                       | 1                       | 2        |                 |        |        |
| 27   | Loganathan| 3                | 0              | 1                | 1                       | 1                       | 1        |                 |        |        |
| 28   | Mahalakshmi| 3                | 0              | 2                | 2                       | 2                       | 3        |                 |        |        |
| 29   | Krishan  | 1                 | 0              | 2                | 2                       | 2                       | 4        |                 |        |        |
| 30   | Palavi   | 5                 | 0              | 2                | 1                       | 1                       | 1        |                 |        |        |
| 31   | Dhanalaksh| 3                | 0              | 3                | 1                       | 1                       | 6        |                 |        |        |
| 32   | Kaitha   | 5                 | 0              | 2                | 2                       | 2                       | 1        |                 |        |        |
| 33   | Ayyalaksh| 2                 | 0              | 1                | 1                       | 1                       | 6        |                 |        |        |
| SNO | NAME     | IMMUNOSUPPRESSION CHIMIO/PROTECTIVE IMMUNOSUPPRESSANTS | RENAL TRANSPLANT DURATION (1-1 M 1-6 M) | SYMPTOMS CHEST SYMPTOMS/FEVER | DURATION 1-5 1-6 1-7 WEEKS | RADIOLOGY | CONSOLIDATION+ | GGO+ | 2 THIN LIN | NODULAR+ | RETICULAR+ | CAVITY+ |
|-----|----------|-----------------------------------------------------|----------------------------------------|---------------------------------|-----------------------------|-------------|----------------|-------|-----------|----------|-----------|--------|
| 34  | GEETHA   | 2                                                   | 0                                      | 2                              | 3                           | 5           |                |       |           |          |           |        |
| 35  | KARTHYAN | 5                                                   | 0                                      | 2                              | 2                           | 2           |                |       |           |          |           |        |
| 36  | DEEPA    | 3                                                   | 0                                      | 2                              | 1                           | 1           |                |       |           |          |           |        |
| 37  | KRISHNAMOORTHY | 5                                           | 0                                      | 3                              | 1                           | 1           |                |       |           |          |           |        |
| 38  | CHITRA   | 5                                                   | 0                                      | 2                              | 2                           | 3           |                |       |           |          |           |        |
| 39  | PARASARATHY | 5                                      | 0                                      | 3                              | 1                           | 1           |                |       |           |          |           |        |
| 40  | GAHARSHAI | 3                                                   | 0                                      | 2                              | 1                           | 6           |                |       |           |          |           |        |
| 41  | ANJALAI  | 1                                                   | 4                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 42  | SUMETHA  | 4                                                   | 2                                      | 2                              | 1                           | 1           |                |       |           |          |           |        |
| 43  | LENDA    | 5                                                   | 3                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 44  | RAVENDRAN | 5                                                   | 0                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 45  | ARIYATHY | 5                                                   | 0                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 46  | RALATHY  | 5                                                   | 0                                      | 2                              | 1                           |             |                |       |           |          |           |        |
| 47  | PERUMAL  | 3                                                   | 2                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 48  | LATHA    | 3                                                   | 2                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 49  | BALAIH   | 2                                                   | 2                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 50  | MENAPPAN | 2                                                   | 0                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 51  | MUKONTAI | 5                                                   | 0                                      | 2                              | 1                           |             |                |       |           |          |           |        |
| 52  | DIALAN   | 3                                                   | 0                                      | 1                              | 1                           |             |                |       |           |          |           |        |
| 53  | VIJAYA   | 2                                                   | 3                                      | 1                              | 2                           |             |                |       |           |          |           |        |
| 54  | PINNITKUT | 3                                                 | 3                                      | 1                              | 2                           |             |                |       |           |          |           |        |
| 55  | VARAVANAVAN | 3                                      | 0                                      | 2                              | 1                           |             |                |       |           |          |           |        |
| 56  | CHANDRA  | 1                                                   | 0                                      | 1                              | 2                           |             |                |       |           |          |           |        |
| 57  | VIJAY    | 5                                                   | 0                                      | 4                              | 1                           |             |                |       |           |          |           |        |
| 58  | RINJA    | 4                                                   | 0                                      | 4                              | 1                           |             |                |       |           |          |           |        |
| 59  | MALLA    | 3                                                   | 0                                      | 2                              | 3                           |             |                |       |           |          |           |        |
| 60  | ILISALAI | 1                                                   | 0                                      | 5                              | 0                           |             |                |       |           |          |           |        |
| 61  | TILASI   | 2                                                   | 0                                      | 1                              | 2                           |             |                |       |           |          |           |        |
| 62  | JAYASHI  | 2                                                   | 0                                      | 2                              | 2                           |             |                |       |           |          |           |        |
| 63  | KALAVATHI| 3                                                   | 0                                      | 5                              | 0                           |             |                |       |           |          |           |        |
| 64  | MINGA    | 3                                                   | 0                                      | 2                              | 2                           |             |                |       |           |          |           |        |
| 65  | RAJESH   | 2                                                   | 1                                      | 4                              | 1                           |             |                |       |           |          |           |        |
| SNO | NAME       | LOBES UPPER | LOBES MIDDLE | LOBES LOWER | LOBES FOCAL | DIFFUSE | GRAMS STAIN | AFB STAIN | GENE XPERT | GENE DETECTED | RF SENSITIVE | RESISTANT | INDETERMINATE | TUBERCULOSIS |
|-----|------------|-------------|--------------|-------------|-------------|---------|-------------|-----------|------------|--------------|--------------|-----------|----------------|-------------|
| 1   | JAYAPALAN  | 3           | 1            | 1           | 3           | 1       | 1           | 1         | 1          | 1            | 1            | 1         | 1              | 1           |
| 2   | CHENANETHU  | 3           | 1            | 1           | 2           | 2       | 2           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 3   | RAGHNE      | 2           | 2            | 1           | 3           | 2       | 2           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 4   | BABUSAN      | 3           | 2            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 5   | CHANDRAHAN   | 2           | 2            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 6   | GOKARAN      | 3           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 7   | PRASAD      | 3           | 2            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 8   | KUMAR       | 2           | 2            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 9   | VISWANATH    | 3           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 10  | SUDHA      | 2           | 1            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 11  | PATIRAM     | 3           | 2            | 2           | 3           | 1       | 1           | 1         | 1          | 1            | 1            | 1         | 1              | 1           |
| 12  | SENTHILKUMAR | 3           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 13  | ANAND      | 3           | 1            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 14  | MAHARAN     | 2           | 2            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 15  | SATYA      | 3           | 2            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 16  | MURALI      | 3           | 1            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 17  | CHANDRAHAN  | 1           | 2            | 3           | 2           | 0       | 2           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 18  | RAGRAHAN    | 2           | 2            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 19  | MURALIYARAG | 2           | 2            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 20  | RAMESH     | 1           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 21  | RAGHUL     | 1           | 1            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 22  | POOJA      | 2           | 2            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 23  | ZETHYAN      | 1           | 1            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 24  | UMA        | 1           | 1            | 2           | 1           | 1       | 1           | 1         | 1          | 1            | 1            | 1         | 1              | 1           |
| 25  | SUNITI     | 2           | 2            | 2           | 1           | 1       | 1           | 1         | 1          | 1            | 1            | 1         | 1              | 1           |
| 26  | VEERARATHNAM | 3           | 2            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 27  | LOGASANAGAN | 3           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 28  | MAHARJAN   | 3           | 2            | 1           | 2           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 29  | KRISHAN    | 3           | 1            | 2           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 30  | PALASH     | 3           | 1            | 2           | 3           | 3       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 31  | DESIAMBAL  | 2           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 32  | KAVITHA    | 2           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| 33  | ANNAIAMBAL | 2           | 1            | 1           | 3           | 2       | 0           | 0         | 2          | 0            | 2            | 0         | 2              | 2           |
| SNO | NAME      | LOBES | GRAMS | AFB | GENE XPERT | RF | TUBERCULOSIS |
|-----|-----------|-------|-------|-----|------------|----|--------------|
|     |           | UPPER| STAN  | POSITIVE | DETECTED | SENSITIVE | POSITIVE |
|     |           | MIDDLE|       | 1    | 2         | 1   | 2            |
|     |           | LOWER |       | 2    | 2         | 2   | 2            |
| 34  | GEETHA    | 2     | 1     | 2    | 2         | 0   | 2            |
| 35  | KARTHIKEYAN| 3     | 1     | 2    | 2         | 2   | 2            |
| 36  | DEEPA     | 1     | 1     | 2    | 2         | 1   | 1            |
| 37  | G Krishnakumar| 2 | 1 | 2 | 2 | 2 | 0 | 2 |
| 38  | GUTHRA    | 1     | 1     | 2    | 2         | 1   | 1            |
| 39  | PARTHASARATHI | 3 | 1 | 1 | 2 | 1 | 3 | 1 |
| 40  | GAURAV SHARMA| 1 | 1 | 1 | 2 | 1 | 1 |
| 41  | ANANDRAJ  | 1     | 1     | 2    | 2         | 0   | 2            |
| 42  | SUMANRAJ  | 1     | 1     | 2    | 2         | 0   | 2            |
| 43  | LETHA     | 3     | 2     | 2    | 2         | 1   | 1            |
| 44  | RAMANAN   | 1     | 1     | 2    | 2         | 1   | 1            |
| 45  | AHANTA    | 3     | 1     | 2    | 2         | 1   | 1            |
| 46  | BALJIT    | 2     | 1     | 2    | 2         | 1   | 1            |
| 47  | PRAMUL    | 1     | 1     | 2    | 2         | 0   | 2            |
| 48  | LATISHA   | 1     | 1     | 2    | 2         | 0   | 2            |
| 49  | RAJASREE  | 1     | 1     | 2    | 2         | 0   | 2            |
| 50  | MEGHANAN  | 3     | 1     | 1    | 2         | 0   | 2            |
| 51  | MEGJEN     | 1     | 1     | 3    | 2         | 0   | 2            |
| 52  | DHANSALI  | 3     | 1     | 2    | 2         | 0   | 2            |
| 53  | VENITA    | 1     | 1     | 2    | 2         | 0   | 2            |
| 54  | FROHINJEE | 3     | 2     | 2    | 2         | 0   | 2            |
| 55  | VARADHARAJAN| 1 | 1 | 2 | 2 | 0 | 2 |
| 56  | CHANDRA   | 1     | 1     | 2    | 2         | 0   | 2            |
| 57  | VIREY     | 1     | 1     | 2    | 2         | 0   | 2            |
| 58  | KIMIKA    | 1     | 1     | 2    | 2         | 0   | 2            |
| 59  | MALA      | 2     | 1     | 2    | 2         | 0   | 2            |
| 60  | SLIMALI   | 2     | 1     | 2    | 2         | 0   | 2            |
| 61  | THULASHI  | 3     | 2     | 2    | 2         | 0   | 2            |
| 62  | JAYANTHI  | 3     | 2     | 2    | 2         | 0   | 2            |
| 63  | KALAVATHY | 3     | 2     | 2    | 2         | 0   | 2            |
| 64  | MENAGA    | 2     | 1     | 2    | 1         | 1   | 1            |
| 65  | RAJESH    | 1     | 1     | 2    | 2         | 0   | 2            |
| SNO | NAME          | BACTERIAL CULTURE POSITIVE=1 | BACTERIAL CULTURE NEGATIVE=2 | FUNGAL CULTURE POSITIVE=1 | FUNGAL CULTURE NEGATIVE=2 | VELD POSITIVE=1 | VELD NEGATIVE=2 | INFECTION NON INFECTION 1=NE 2=BI 3=B+ 4=MIXED |
|-----|---------------|------------------------------|-----------------------------|---------------------------|---------------------------|-----------------|-----------------|-----------------------------------------------|
| 1   | JATAP ALAN    | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 2   | CHELAMOTHU    | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 3   | RAJARI        | 1                            | 2                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 4   | RAVICHANDERAN | 2                            | 0                           | 2                         | 0                         | 2               | 0               | 0                                                             |
| 5   | CHANDRAHANAN  | 1                            | 1                           | 3                         | 0                         | 1               | 1               | 1                                                             |
| 6   | GANESHEKAR    | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 7   | PRAGASH       | 1                            | 3                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 8   | IGAR          | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 9   | VELAVISHEM    | 1                            | 4                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 10  | SPOSHY       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 11  | PATHYAKSHA    | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 12  | KANDerekar    | 1                            | 2                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 13  | ASOHAN        | 2                            | 0                           | 1                         | 3                         | 1               | 1               | 3                                                             |
| 14  | MOHANAN       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 15  | SATYA         | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 16  | MOHANAN       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 17  | CHANDRAHANAN  | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 18  | RAJENDRAN     | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 19  | MEHAL JAYAJAN | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 20  | RAMISH        | 1                            | 1                           | 3                         | 0                         | 1               | 1               | 2                                                             |
| 21  | RAGHN          | 2                             | 0                          | 1                         | 5                         | 1               | 1               | 3                                                             |
| 22  | POOLIA        | 1                            | 0                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 23  | JETACHANDRAON | 2                            | 0                           | 1                         | 1                         | 1               | 1               | 3                                                             |
| 24  | LIMA           | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 25  | Shanthi       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 1                                                             |
| 26  | VENIKAHARATAN  | 1                           | 2                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 27  | LOGANKHAN     | 1                            | 5                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 28  | MOHAJANSHI    | 1                            | 4                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 29  | ERIKSON       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 30  | PALAN         | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 31  | DASAMAL       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 0                                                             |
| 32  | SANTHA        | 1                            | 2                           | 2                         | 0                         | 1               | 1               | 2                                                             |
| 33  | ATTAMAL       | 2                            | 0                           | 2                         | 0                         | 1               | 1               | 3                                                             |
| SNO | NAME        | BACTERIAL CULTURE POSITIVE | Fungal Culture POSITIVE | Yeard Positive | Infection Non Infection | Infections Bacterial | Infections Fungal | Infections Mixed |
|-----|-------------|-----------------------------|--------------------------|----------------|------------------------|---------------------|-------------------|------------------|
| 34  | GRETHA      | 1                           | 5                        | 1              | 1                      | 1                   | 1                 | 4                |
| 35  | KARTHIKAN   | 2                           | 0                        | 2              | 0                      | 2                   | 0                 | 0                |
| 36  | DEEPA       | 1                           | 6                        | 2              | 0                      | 1                   | 1                 | 4                |
| 37  | SREEMAMORTY | 2                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 38  | CHIRA       | 2                           | 0                        | 0              | 2                      | 0                   | 1                 | 1                |
| 39  | PRAKASHARATI| 1                           | 3                        | 0              | 1                      | 1                   | 1                 | 4                |
| 40  | GAURAV SHAIK| 1                           | 2                        | 1              | 1                      | 1                   | 1                 | 4                |
| 41  | ASANDRAI    | 2                           | 0                        | 0              | 1                      | 1                   | 1                 | 3                |
| 42  | SUNITA      | 3                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 43  | LIDIA       | 2                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 44  | RAJENDRAN   | 2                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 45  | ARUNA       | 2                           | 0                        | 1              | 7                      | 1                   | 1                 | 4                |
| 46  | BALAJI      | 2                           | 0                        | 0              | 1                      | 7                   | 1                 | 4                |
| 47  | PRAVAN      | 2                           | 0                        | 0              | 2                      | 0                   | 2                 | 0                |
| 48  | LATHA       | 1                           | 6                        | 2              | 0                      | 1                   | 1                 | 2                |
| 49  | ISAVI       | 1                           | 1                        | 1              | 5                      | 1                   | 1                 | 4                |
| 50  | MENAPAN     | 1                           | 2                        | 1              | 5                      | 1                   | 1                 | 4                |
| 51  | MINSAN      | 1                           | 1                        | 2              | 0                      | 1                   | 1                 | 2                |
| 52  | DHRANAL     | 2                           | 0                        | 0              | 1                      | 1                   | 2                 | 0                |
| 53  | VERITY      | 2                           | 0                        | 0              | 1                      | 2                   | 0                 | 0                |
| 54  | PUNNASAGODI | 1                           | 6                        | 2              | 0                      | 1                   | 1                 | 2                |
| 55  | VARACHARGADAL| 3                          | 0                        | 0              | 1                      | 2                   | 0                 | 0                |
| 56  | CHIDRA      | 2                           | 0                        | 2              | 0                      | 1                   | 2                 | 0                |
| 57  | VIFT       | 1                           | 1                        | 2              | 0                      | 1                   | 1                 | 3                |
| 58  | RENAGA     | 2                           | 0                        | 1              | 6                      | 1                   | 1                 | 3                |
| 59  | MESAAL     | 2                           | 0                        | 2              | 0                      | 2                   | 0                 | 0                |
| 60  | ELHAMAL    | 3                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 61  | TMRAHI      | 2                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 62  | JENATANI   | 3                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 63  | KALAVADHY  | 2                           | 0                        | 0              | 2                      | 0                   | 0                 | 0                |
| 64  | MENAKA      | 3                           | 0                        | 0              | 2                      | 0                   | 0                 | 1                |
| 65  | RAJESH      | 2                           | 0                        | 1              | 1                      | 1                   | 1                 | 3                |
| SNO | NAME       | COMPLICATIONS HYPOXIA=1 | BLEEDING=1 | PNEUMOTHORAX=3 | COMPLICATION YES=1 NO=1 | TREATMENT MODIFIED YES=1 NO=1 | TMT ATT=1 ANTIBIOTICS CHANGED=2 UNCHANGED=3 | CHIMOTHERAPY STARTED=3 | FOLLOW UP IMPROVED=1 LOST=2 ON FOLLOW UP=3 | NON IMPROVED=12 NON IMPROVED=LOST |
|-----|------------|-------------------------|------------|-----------------|--------------------------|-------------------------------|---------------------------------------------|---------------------------------|------------------------------------------|-----------------------------------|
| 1   | JAYAPALAN  | 0                       | 2          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 2   | PRINAMITHU  | 1                       | 1          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 3   | RAJASEKHAR  | 0                       | 3          |                 | 2                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 4   | RANJANRAJAN | 0                       | 2          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 5   | GANANARAVAN | 1                       | 1          |                 | 1                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 6   | RAMESH      | 0                       | 2          |                 | 1                        | 3                             | 1                                           | 1                               | 1                                         | 1                                 |
| 7   | RAMESH      | 1                       | 1          |                 | 1                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 8   | KUMAR       | 0                       | 3          |                 | 2                        | 4                             | 1                                           | 1                               | 2                                         | 2                                 |
| 9   | VELAVYIYER  | 0                       | 2          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 10  | SUGANITA    | 0                       | 3          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 11  | PATROVANIA   | 0                       | 2          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 12  | SANTHARAJ  | 1                       | 1          |                 | 1                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 13  | ANANTHAN    | 1                       | 1          |                 | 2                        | 4                             | 2                                           | 2                               | 2                                         | 2                                 |
| 14  | MADABAN     | 1                       | 1          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 15  | SATYA       | 0                       | 2          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 16  | MAHETAN     | 0                       | 2          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 17  | CHANDRASEKAR | 0                      | 3          |                 | 1                        | 5                             | 1                                           | 1                               | 1                                         | 1                                 |
| 18  | RAJARAN     | 3                       | 1          |                 | 1                        | 1                             | 2                                           | 1                               | 1                                         | 1                                 |
| 19  | MURALESHKAN | 0                       | 2          |                 | 1                        | 2                             | 2                                           | 2                               | 2                                         | 2                                 |
| 20  | RAMAKRISHAN | 0                       | 2          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 21  | RASHELA     | 0                       | 2          |                 | 1                        | 3                             | 1                                           | 1                               | 1                                         | 1                                 |
| 22  | POOJA       | 3                       | 1          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 23  | SITAMACHANDAN | 2                     | 1          |                 | 2                        | 4                             | 2                                           | 2                               | 2                                         | 2                                 |
| 24  | TAHA        | 0                       | 3          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 25  | SHANTI      | 0                       | 3          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 26  | GENKATANATHAN | 0                    | 3          |                 | 1                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 27  | LOGANATHAN  | 1                       | 1          |                 | 1                        | 2                             | 1                                           | 1                               | 1                                         | 1                                 |
| 28  | MADALASSHMI  | 0                      | 3          |                 | 3                        | 5                             | 1                                           | 1                               | 1                                         | 1                                 |
| 29  | KHEHAN     | 0                       | 3          |                 | 2                        | 3                             | 4                                           | 1                               | 1                                         | 1                                 |
| 30  | PALAN       | 2                       | 1          |                 | 2                        | 4                             | 1                                           | 1                               | 1                                         | 1                                 |
| 31  | DEEAMAL    | 0                       | 3          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| 32  | KANGAN     | 0                       | 2          |                 | 1                        | 2                             | 4                                           | 1                               | 1                                         | 1                                 |
| 33  | NAVYAMAL   | 0                       | 3          |                 | 1                        | 1                             | 1                                           | 1                               | 1                                         | 1                                 |
| SNO | NAME     | COMPLICATIONS | TREATMENT | FOLLOW UP |
|-----|----------|---------------|-----------|-----------|
|     |          | NE=1 HYPOXEMIA=1 BLEEDING=1 PNEUMOTHORAX=1 | MODIFIED YES=1 NO=2 | IMPROVED=1 NON IMPROVED=DIED=LOST |
| 34  | GREETHA  | 0 2           | 1 3       | 2         | 2         |
| 35  | EARTHRIYA | 0 2           | 2 4       | 1         | 1         |
| 36  | DEEPA    | 0 2           | 1 1       | 2         | 2         |
| 37  | GHENAMORTHI | 0 2       | 1 1       | 2         | 2         |
| 38  | CHITA    | 0 2           | 1 1       | 2         | 2         |
| 39  | PARIHASARATHY | 1 1       | 1 1       | 2         | 2         |
| 40  | GAHRISHRAJ | 0 2           | 1 1       | 2         | 2         |
| 41  | ANANDRAJ | 0 2           | 1 3       | 2         | 2         |
| 42  | SUMITHRA | 0 2           | 2 4       | 3         | 3         |
| 43  | LIDWA    | 0 2           | 1 1       | 2         | 2         |
| 44  | RAVINDERAN | 0 2       | 1 1       | 2         | 2         |
| 45  | ARNATA   | 1 1           | 1 1       | 2         | 2         |
| 46  | RAJITH   | 0 2           | 1 1       | 2         | 2         |
| 47  | PERIMAL  | 0 2           | 2 4       | 1         | 1         |
| 48  | LATHA    | 0 2           | 2 6       | 1         | 1         |
| 49  | EMAR     | 0 2           | 1 3       | 1         | 1         |
| 50  | MENAPPAN | 0 2           | 1 3       | 1         | 1         |
| 51  | MERIGAN  | 0 2           | 2 4       | 1         | 1         |
| 52  | DRAHAPAL | 2 1           | 1 5       | 3         | 2         |
| 53  | VERITA   | 0 2           | 1 5       | 3         | 2         |
| 54  | PUNNAMADDI | 0 2       | 2 4       | 1         | 1         |
| 55  | VASRALAHA | 2 1           | 1 5       | 3         | 2         |
| 56  | CHANDRA  | 0 2           | 1 5       | 4         | 2         |
| 57  | VIJAY    | 0 2           | 2 4       | 1         | 1         |
| 58  | RISHA    | 0 2           | 1 3       | 1         | 1         |
| 59  | MOLA     | 0 2           | 2 4       | 1         | 1         |
| 60  | KUMALAI  | 0 2           | 2 6       | 1         | 1         |
| 61  | THILASH  | 0 2           | 2 4       | 1         | 1         |
| 62  | JESTADHU | 0 2           | 2 4       | 1         | 1         |
| 63  | KALAVATHY | 0 2       | 2 4       | 1         | 1         |
| 64  | MANIKAR | 0 2           | 1 4       | 3         | 2         |
| 65  | RAVESH   | 1 2           | 1 3       | 4         | 2         |