A Dissertation on

A Study of Drug Resistance TB among patients with New Sputum Smear Positive Pulmonary Tuberculosis

Dissertation Submitted to

THE TAMILNADU Dr.M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

With partial fulfillment of the regulations

for the award of the degree of

M.D. GENERAL MEDICINE

BRANCH-I

COIMBATORE MEDICAL COLLEGE,

COIMBATORE

APRIL 2016

CERTIFICATE

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Dissertation Topic : A STUDY OF DRUG RESISTANCE TB AMONG PATIENTS WITH NEW SPUTUM SMEAR POSITIVE PULMONARY TUBERCULOSIS.

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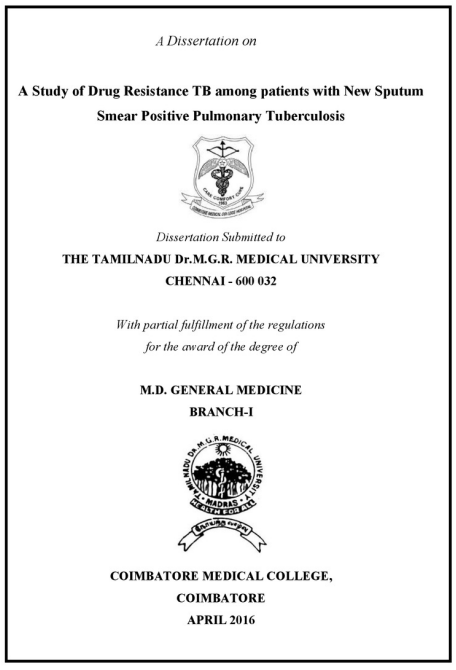

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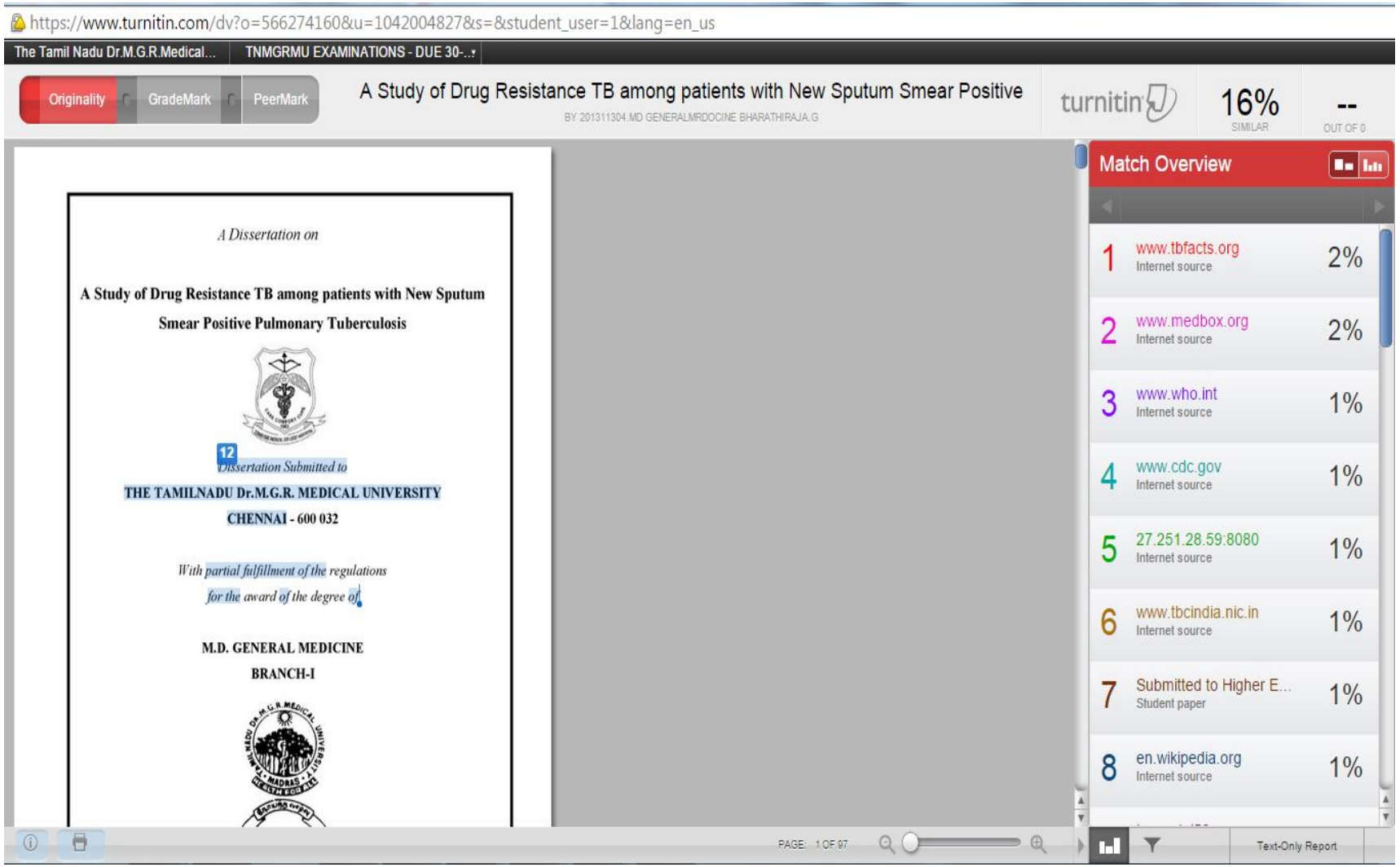
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DECLARATION

I solemnly declare that the dissertation titled **"A Study of Drug Resistance TB among patients with New Sputum Smear Positive Pulmonary Tuberculosis"** Was done by me from JULY 2014 to JULY 2015 under The guidance and supervision of HOD & Professor **Dr.KUMAR NATARAJAN M.D.** This dissertation is submitted to **The Tamilnadu Dr. M.G.R. Medical University** towards the partial fulfillment of the requirement for the award of MD Degree in General Medicine (Branch I).

Dr.BHARATHIRAJA.G

Place: Coimbatore

Date:

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Dr. BHARATHIRAJA. G

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ABBREVATIONS AND ACRONYMS

AFB	- Acid fast bacilli
AM	- Alveolar Macrophage
CP	- Continuation Phase
CPC	- Cetyl Pyridinium Chloride
Cs	- Cycloserine
DOTS	- Directly observed treatment short course
ESR	- Erythrocyte Sedimentation Rate
GoI	- Government of India
H	- Isoniazid
HIV	- Human Immunodeficiency Virus
INH	- Isoniazid
IRL	- Intermediate Reference Laboratory
IP	- Intensive Phase
IRL	- Intermediate Reference Laboratory
Km	- Kanamycin
Lfx	- Levofloxacin
LJ	- Lowenstein Jensen
MDR-TB	- Multidrug-resistant Tuberculosis
MIC	- Minimal Inhibitory Concentration
PAS	- *p*-aminosalicylic acid
Ofx	- Ofloxacin
R	- Rifampicin

RNTCP	- Revised National TB Control Programme
S	- Streptomycin
SGOT	- Serum Glutamic Oxalo acetic Transamnase
SGPT	- Serum Glatamic Pyruvatr Transaminase
TB	- Tuberculosis
UV Light	- Ultra Violet Light
WHO	- World Health Organization
X-DR	- Extensively Drug Resistance
Z	- Pyrazinamide

INTRODUCTION

Tuberculosis (TB) is an infectious disease which spread by Mycobacterium tuberculosis. TB primarily usually infect the lungs which is called as Pulmonary TB (PTB). It also affects intestines, meninges, bones and joints, lymph nodes, skin and all other parts of the body. Tuberculosis usually presented with features like cough with or without expectoration associated with blood (Haemoptysis), intermittent low grade evening rise of temperature , appetite and weight loss, chest pain .

Tuberculosis is one of the main diseases of low socioeconomic status along with HIV. A one third of world's peoples is found to be affected by M. Tuberculosis, its infects others by rate of one per second. It is the infection of poor mostly on the young adults . The most of the TB mortality were happened in the developing world. If the person was untreated with active TB disease will infect approximately almost ten to fifteen peoples every year and this causes spread of TB.

The peoples having HIV Disease are most commonly to develop TB. The risk of infection of TB in persons with DM, Chronic disease which leads to immune-compromised, low economic status, smokers are high. The Estimation of prevalence of drug resistance for TB in the community will be useful for creating new policies and treatment with effective drugs to complete cure and it will avoid the development of drug resistance.

Drug resistance TB is the burden of illness in the society with several constraints in the management of TB patients. Using of Highly effective regimens utilizing the drugs that have not been prescribed previously and known to posses good anti mycobacterium activity needs to be implemented , which increases operational expenses in drugs and its distribution, monitoring the toxicity of the drugs and supervision of the administration of drugs to ensure the intake regularly. Though the efficacy of the drugs in the management of pulmonary tuberculosis is well established , and its application on a mass level under the home based treatment programme gives much worries due to operational difficulties. With the poor drug compliance of patients causing markedly increases in number of patients having drug resistant TB bacilli in the community.

Tuberculosis is the disease treatable with a full course of Anti TB drugs. Multi Drug Resistance Tuberculosis (MDR-TB) is described as the resistance to anyone of the first-line TB drugs Rifampicin and Isoniazid. The Extensively drug-resistant TB (XDR-TB) is called because of resistant of drugs to the 3 or more than three of the 6 types of second-line drugs. This is a matter of global concern.

AIMS

This study mainly focuses on the detection, comparison of prevalence of MDR-TB among New smear sputum Positive TB patients. And To determine the pattern of drug resistance in them.

OBJECTIVES

- To determine the prevalence of Drug resistance in New smear sputum positive patients during study period.
- To determine the drug resistance to Rifampicin among them by using Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) [GeneXpert] .
- To analyze the drug resistance of New smear sputum positive Patients to decide whether the DOTS PLUS regimen should start early.

REVIEW OF LITERATURE

"I have no business to live this life if I cannot eradicate this scourge from mankind"-Robert Koch (Delivering a lecture at Berlin University on his discovery of tuberculosis bacilli, 1882)[1].

HISTORY

The ancient human strains shows the evidence of the tuberculosis infection were more than 9,000 B.C years old[4] . Greek term phithisis known as tuberculosis, in around 460 BC, Hippocrates found that the phthisis[5] was the dangerous disease of the times involving cough with blood and fever, it almost end with mortality[2]. It is spreads from person to person via droplets or sputum from the people with the acute TB disease. It is also known as Koch's disease, after the scientist Robert Koch[1]. The bacteria causing TB, Mycobacterium tuberculosis, was identified and described on 24 March (the day called as World TB Day) 1882 by Robert Koch[6] . The first immunization for tuberculosis was developed from attenuated bovine-strain tuberculosis by Albert Calmette and Camille Guerin in 1906. It called as "BCG" (Bacillus of Calmette and Guerin)[7] .

EPIDEMIOLOGY

TB is a major public health problem in our country[9]. TB is the commonest cause of mortality due to single infectious agent[9]. It nearly kills about the more than 100000 peoples including children each and every year[10]. Every second someone in the world infecting with tuberculosis[8].

BASIC EPIDEMIOLOGICAL PRINCIPLES:

Measures of Tuberculous Infection

- ✓ Prevalence of infection
- ✓ Risk of infection
- ✓ Annual risk of infection

Measures of Tuberculosis disease:

- ✓ Incidence of tuberculosis disease
- ✓ Prevalence of tuberculosis disease
- ✓ Risk of developing TB disease

TUBERCULOSIS DISEASE BURDEN-GLOBAL

Tuberculosis (TB) is the most world's worst communicable diseases. In 2013, there was an estimated about Nine millions people had TB and, One and Half million expired due to this disease, in that nearly 4 million were HIV-positive. TB incidence has been decreasing in every year and it is estimated that 37 million people was rescued from the year 2000 and 2013 with good diagnosis and treatment. Most of the TB mortality are avoidable, the number of mortality are from the disease is still in much in number and steps to fight is should be improved if 2015 global targets and the Millennium Development Goals (MDGs), are have to achieved.

TB is seen in every part of the globe, the Global Tuberculosis Report 2014 gives data from 202 countries .This shows worldwide total number of new TB cases and deaths in 2013 and more than previous years[11].

A special report of year 2014 showed the progress has been done in control and management of drug resistant TB in past twenty years, and results of national and international levels in recent years. In the World, identification of the new cases with multidrug-resistant TB (MDR-TB) was 3.5% in 2013 and which did not altered compared with last few years[11].

TUBERCULOSIS BURDEN IN INDIA

With the population of India about 125 crores and the biggest country in the Region. It is ranked first in the high economically affected countries due to TB and gives 24% of the calculated TB cases in the world wide and about 20% of deaths in the world wide in the year 2013. India having the more economically affected due to TB in the world, an estimated two million cases per year, which is one fifth of the global census[12].

India having about Forty percent of people are infected with MTB , the most majority having latent TB than other. And also statement given by the World Health Organisation (WHO), the three million peoples are expiring from TB every year in our country. GOI provides services through Revised National TB Control Programme, and also by private health facilities[12].

DRUG RESISTANT TB IN INDIA

In India drug resistance TB seen more frequently and its presents propably from the time anti TB drugs were started for TB. The prevalence of multi drug resistant (MDR) TB has thought , very less in our country. Number of the studies showed the MDR TB occurrence about 3% in new cases and around

12-17% in retreatment cases. Even very less number of cases it will spreads to more numbers[13].

MDR-TB prevalence is estimated to low (2.2% among new cases and 15% among retreatment cases) based on The sub-national DRS conducted in three states between 2006 and 2009 the prevalence of MDR TB was showed as 2.2% in new cases and 15% in the old cases[11] . RNTCP combined with WHO started the National Anti tuberculosis Drug Resistance Survey 2014–2015 in a sample of both newly diagnosed Cat I sputum smear-positive PTB cases and previously treated Cat II sputum smear-positive PTB cases. Inspite of less prevalence , due to the large peeples and number of TB cases identified every year[12], India comes as first among the 27 countries in the world, and sharing the 21% of all MDR-TB. RNTCP had a plans to improve the MDR-TB services to manage nearly Forty thousand MDR-TB patients in in India every year by 2017[12].

In India all the services is provided by the Revised National TB Control Programme and also by the private practioners and hospitals.

PREVENTION OF MDR TB

It has been well known to all the health care people that adequate management practices will leads to this resistance. Areas which has very less TB control are having the high incidence of MDR TB. RNTCP doing that implementation of highly efficient DOTS Programme for the control of TB for our country[16]. Prevention of MDR-TB in the country has been much important than its management. Its not possible to challenge the MDR TB with treatment

only, each and every MDR-TB cases cost twenty times expensive than the usual TB case. So, the TB diagnosis and treatments should prioritized with the uses of DOTS to reduces the spread and control of the MDR-TB[16].

CAUSES OF DRUG-RESISTANT TUBERCULOSIS

Drug-resistant tuberculosis having the microbiological, clinical and programme failure reasons. In microbiological view , the MDR TB is caused due to the mutation in the genes which makes drug inability and inefficacy against that mutant bacilli[11]. An irregular and poorly provided treatment regimen which gives rise to drug resistant mutants, it gives rise as a dominant strain of the infected patients.

However MDR TB is a man-made problem because of the inadequate treatment, ineffective drugs and very less drug adherence leads to the cause of MDR TB development[11](Table-1).

TABLE - 1

CAUSES OF MDR TB

Providers/Programmes	Drugs	Patients
Inadequate regimens	**Inadequate supply/quality**	**Inadequate drug intake**
1.Absence of guidelines or indequate guidelines **2.Non- Compliance with guidelines** **3.Inadequate training of health staff** **4.No monitoring of treatment** **5.Poorly organized or funded**	**1.Un availability of some drugs.** **2.Poor quality** **3.Poor storage conditions** **4.Wrong combinations and dosages.**	**1.Poor drug compliance.** **2.Lack of information** **3.Non availability of free drugs** **4.Adverse drug reactions** **5.Socio-economic barriers** **6.Mal-absorption** **7.Substance abuse**

Revised National Tuberculosis Programme (RNTCP)[16]

GOI , WHO and the World Bank are all reviews the National Tuberculosis Programme (NTP) in the year 1992. Which gives the revised strategy for NTP was evolved.

Alterations are done in RNTCP as follows:

1. Case finding should be passive with the good sputum microscopy.
2. Differentiation of patients.
3. Improve the quality of Management.
4. The management with full course should be ensured before starting the dugs by patient wise containers (tablets should be given without interruption).
5. Confirm the intake of drugs by treatment observer.
6. Patients should Regularly followed for sputum examination.
7. Services to the patients should nearby home.
8. Outcome of management should be evaluated .
9. Patients' education should must.
10. Laboratory quality control.

The Aims and Objective of RNTC[16] are:

1. Target the not < 85 % cure rate of cases of by the short course chemotherapy in periphery areas.
2. Finding of the 70 % cases by the sputum microscopy.
3. Involvement of non-governmental organizations (NGOs)
4. Directly Observed Treatment Short Course (DOTS) a community based TB treatment and care strategy .

TB control has been depends upon the prevention of transmission of the infectious agent. These has to be achieved by finding the people those having TB and treating them, Hence they cannot spread the disease anywhere. Number of concepts in the DOTS developed by Dr.Karel Styblo in the form of research done in India at the Tuberculosis Research Centre (TRC) Chennai and the National TB Institute (NTI) Bangalore.

Observations from above:

a. TB patients are not be inpatients and they can treated at home.

b. In DOTS where patients should be observed to taking the drugs was essential.

c. Medications taking 3 times a week are useful, effective.

d. Sputum microscopy was helpful in a case identification.

REVISED RNTCP TARGETS (2012-2017)[18]

In 2010 the RNTCP announces the major policy revision to create the idea, to adopt the concept of Universal access to good quality diagnosis and management for all TB patients in our country. This guides extension of the reach of RNTCP to people who diagnosed with TB, and also to improve the services already running.

THE AIMS ARE TO ACHIEVE THE FOLLOWING TARGETS BY THE END OF 2015[18]:

- Early case finding and the management of minimum of 90% of TB cases in society, including HIV associated TB
- Screening for drug resistant TB should be done for all retreatment smear-positive TB patients, services to be provided for multi drug resistant TB

- HIV counseling, testing should be carried out for all TB patients and HIV infected TB patients should gives the HIV care and support.
- Successful outcome about minimum 90% of all new TB patients, and at least 85% of all already treated patients
- The extension of RNTCP services to diagnose and treat all those patients attends in the private hospitals.

THE RNTCP PLANS TO ACHIEVE THESE TARGETS BY:

- Using rapid diagnostics for the diagnosis of TB and drug resistant TB
- Expanding services for the management of multi drug resistant TB
- Urban TB control to be strengthened
- Improving the public-private partnerships
- Strengthening of the quality of DOTS services
- Cooperate with National Rural Health Mission supervision.

PRIORITIES FOR THE MANAGEMENT OF MDR TB IN INDIA

Drug resistant TB increased due to the poor drug compliance of the patients, than they directly affected with MDR TB strain. A magnificent quality DOTS program, and will prevent the prevalence of the resistance by supervision them. The DOTS-Plus regulations gives that current drug resistant strains were gives new drug resistant cases, and that rightly identification of MDR TB cases and the management with correct line of management are important to hold transmission, apart from humanitarian views of providing appropriate treatment for people with drug resistant TB. Inspite of this the

DOTS-Plus guidelines emphasis that the basic DOTS programme without the MDR contents should be continue to the priority for TB control for our country. In add to that in every DOTS implementing unit in India, DOTS should also to give important to the DOTS-Plus[19].

However the target was to treating 30,000 MDR TB cases yearly by 2012-2013, by the end of 2011 just 10,267 MDR patients was diagnosed, and only 6,994 was got treatment. However, it is clear that progress is being made, as in Mumbai it was said in June 2013 that 3,600 patients were being treated for MDR TB, whereas 2 years before Mumbai was treated for 280 patients only[11].

TOTALLY DRUG RESISTANT TB IN INDIA

Resistant to all the first and second line TB drugs is called as Extremely drug resistant TB . It is not possible to treat. In January 2012 it was reported that twelve cases of this type of TB had been reported in Mumbai[18].

ETIOLOGICAL AGENT

Mycobacterium Tuberculosis is the causative agent of the tuberculosis, which belongs to the family Mycobacteriaceae, order of Actinomycetales and the genus mycobacterium. Mycobacterium tuberculosis species belonging to the M.Tuberculosis complex which is the commonest etiological agent causing disease in Humans[20].

Mycobacterium tuberculosis is a rod-shaped, non spore-forming, thin bacterium 0.5micro meter by 3 micro meter. (fig.1)

Mycobacterium tuberculosis is acid fast bacilli, because of organisms content rich of mycolic acids, long chain cross linked fatty acids and other cell-wall lipids.

Most of the antibiotics are not effective against TB because mycobacterial cell wall, contains lipids which are joined underlying arabinogalactan and peptidoglycon, this structure gives low permeability of the cell wall, which takes part in the host-pathogen interaction and facilitates the survival of the tubercle bacilli inside the phagocytes

FIGURE 1

MYCOBACTERIUM TUBERCULOSIS[21]

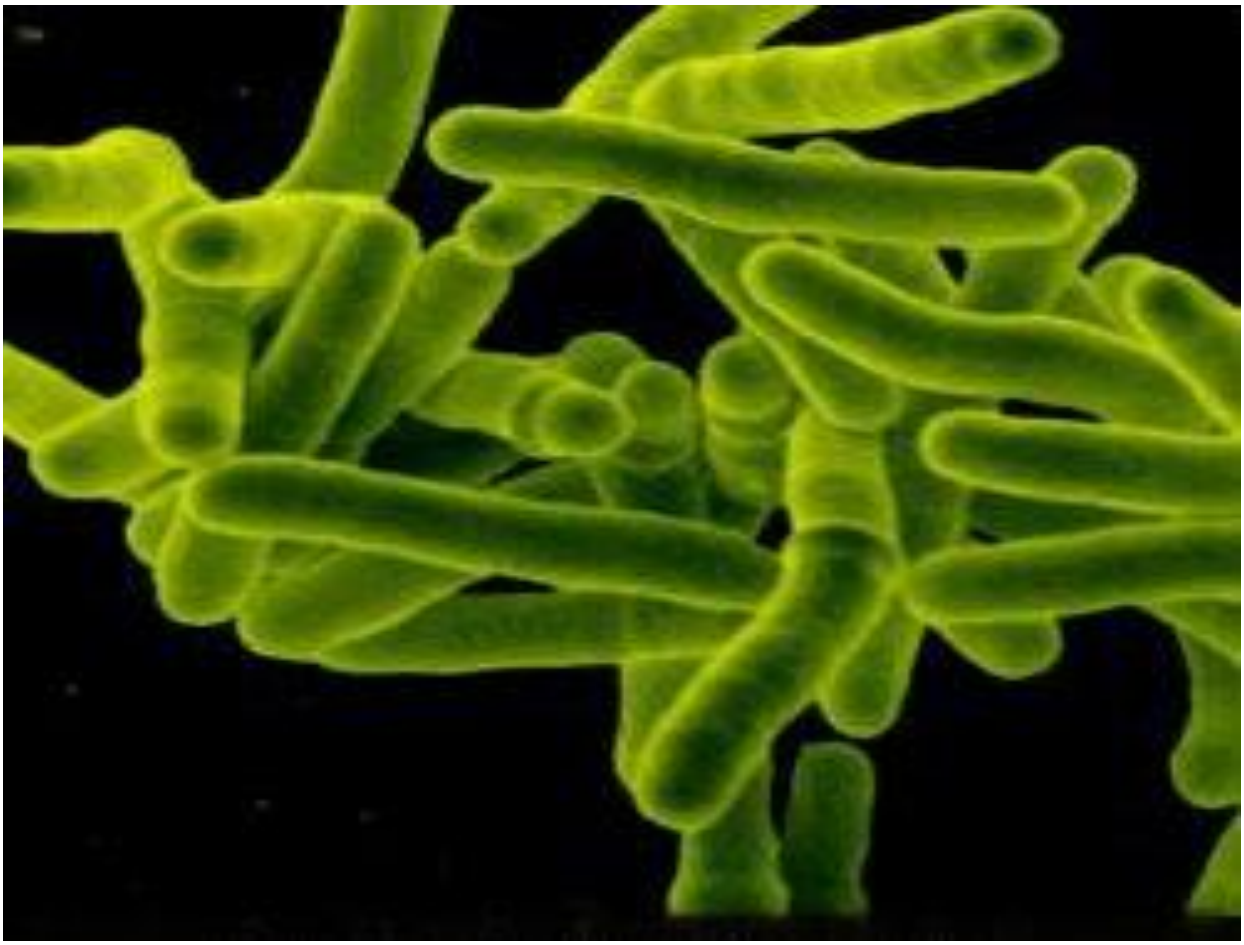
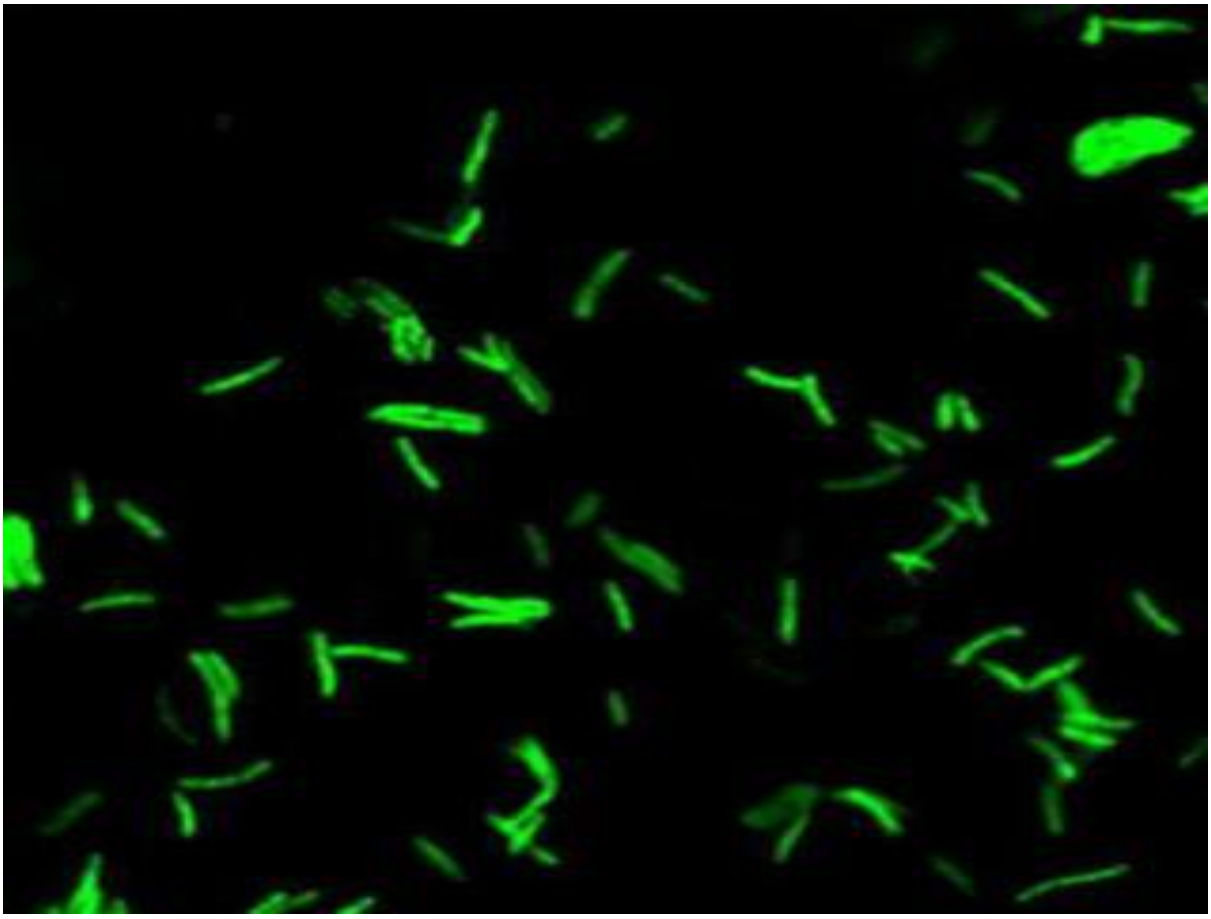


FIGURE 2

MTB IN AURAMINE- RHODAMINE STAINING[21]



MODE OF TRANSMISSION

TB mainly transmitted through aerosol.The bacteria are spreads from person to person in tiny microscopic droplets when a TB sufferer coughs, sneezes, speaks, sings, or laughs. The people with active PTB are spread the bacteria to others[20].

Table 2.

FACTORS WHICH INFLUENCE THE SPREAD ARE[22]:

1.Virulence of the bacilli
2.Number of bacilli in the droplets
3.Ventilation
4.Exposure of TB bacilli to sun light
5.Immune status of the exposed person
6.Proximity, frequency and duration of exposure to the TB patient

SYMPTOMS

Initial symptoms of active TB can include loss of weight, fever, sweats in the night, and loss of appetite. Symptoms may be not noticed by infected person. For somebody, the disease either goes into remission or chronic and more with cough, chest pain, and bloody sputum (saliva)[20]. Symptoms of TB involving areas other than the lungs, depends on the organ area affected

PATHOLOGY OF TUBERCULOSIS[23]

Inhalation of bacilli rich droplets leads to seeding of the airways. The bacilli in these droplets are trapped within the mucus of the upper airways. This mucus is produced by goblet cells and it serves to catch foreign particles. This is the primary defence mechanism preventing infections by many airborne pathogens. But a significant percentage of the bacteria manage to reach the alveoli within the lungs bypassing the mucus barrier. Alveoli contain alveolar macrophages which are very potent and engulf the invading TB bacilli. These macrophages are part of the innate immune system and kill at first contact.

In the uptake of mycobacteria by macrophages, mycobacterial lipoarabinomannan is an important component. Complement system has a role to play in the phagocytises of bacteria as well.

These successive events lead to distinct possibilities:

1) Latent tuberculosis – which follows control of infection.
2) Primary progressive tuberculosis – which implies progression to active disease.

Whenever mycobacterium enters the lung the manifestation of the disease is fully depends on the body immunity system. If an infected person is well immune the spread or further development of the disease will be limited to the primary site of infection. When bacilli reach the alveoli the first defence which comes into action is alveolar macrophages (AM) and the bacilli will be taken into the AM, with the help of proteolytic enzymes and cytokines AM will tries to lyse the bacilli. But mycobacterium continues to multiply inside the AM, released cytokines from the AM will represent the mycobacterium antigen to T-lymphocytes (T lymphocytes are belongs to cell mediated immunity)

Next stage is the formation of the granuloma (figure 3.4), which is formed by the accumulation of the T-lymphocytes along with the AM. Formation of granuloma (nodular lesion) will take to 2 to 12 weeks. This is how body immune system will contain the bacilli from spreading to other sites and also multiplication of the bacilli.

These will be destruction of the macrophages inside the granuloma forming solid necrosis. And subsequently there will be formation of the cheesy material inside the granuloma called as caseous necrosis. This contains low

oxygen, low ph and deficient in nutrients, again it limits the spread and multiplication of the Bacilli but it can survive inside the granuloma for linger period. In immuno compromised persons there will be spillage of the bacilli out of the granuloma and may spread to other part of the body, may form cavity, may spread through the blood to cause milliary tuberculosis and extrapulmonary tuberculosis.

CLINICAL MANIFESTATIONS

Based on the immunity status of the patient, tuberculosis can present in various ways.

The different stages are

- Latent tuberculosis
- Primary disease
- Primary progressive disease
- Extra pulmonary disease

Each stage will manifest with varied clinical manifestations[24].

LATENT TUBERCULOSIS

Those patients who present with latent TB, are not infectious, not toxic, and do not present with any signs and symptoms of the disease. The necrotic material consists of viable tuberculous bacilli and which can persist for years and which can become reactivated later when the immune system becomes defective. Various conditions predispose to a compromised immune system such as malnutrition, old age, uncontrolled diabetes, HIV disease, long term steroid use, smoking, organ transplantation and chemotherapy.

PRIMARY DISEASE

Primary tuberculosis presents mostly in a sub-clinical stage and is mostly asymptomatic. However some self-limiting findings may be elicited on detailed examination. Lymphatic spread may lead to occurrence of paratracheal lymphadenopathy. Primary disease can also present as a pleural which is a distinguished finding. The tuberculous bacilli enter the pleural space from adjacent area to cause effusion. It can remain asymptomatic or can increase progressively leading to symptoms like fever, breathlessness and pleuritic type of chest pain. Signs of effusion like, diminished breath sounds, stony dull note on percussion, decreased vocal resonance and vocal fremitus when present implies that excess has entered the pleural cavity.

PRIMARY PROGRESSIVE DISEASE

Only 5-10% of people exposed to Mycobacterium tuberculosis develop active tuberculosis. The early symptoms and signs of active tuberculosis are non-specific. Some present with features such as malaise, weight loss, and low grade fever associated with chills and night sweats and progressive fatigue. Wasting is an important feature of active disease and includes loss of lean and fat tissue and muscle mass. It can be attributed to the lack of appetite and to the increase in the inflammatory markers leading to altered metabolism. Poor oxygenation can lead to hypoxia causing finger clubbing at later stages. Most of the patients develops cough eventually. Initially cough may be non productive, but later turns productive to purulent and occasionally be mixed with blood also. Hemoptysis can occur due rupture of a vessel in the cavity, destruction of vessel in the wall of

the cavity or after the formation of aspergilloma within the cavity. Pleuritic chest pain may occur due to inflammation of the parenchyma. Patient can have rules especially during inspiration, over the involved areas. Patient may present with dyspnea and orthopnea in extensive disease. Lab values may show anemia which can cause easy fatiguability and also show leucocytosis,

EXTRA PULMONARY TUBERCULOSIS

The risk of developing secondary disease with immuno suppression and is present in only 20% of immuno competent individuals. Tuberculous lymphadenopathy is the most presentation and the central nervous system provides for the most dangerous location which can lead to meningitis or space occupying tuberculomas. High risk groups after being exposed to cases can present with headache and altered sensorium and considered in the differential diagnosis. Extra pulmonary tuberculosis can also infects bloodstream and lead to milliary or disseminated tuberculosis. The disease can involve multiple organs after the bacilli spreads throughout the blood. There is rapid progression seen in milliary tuberculosis and it becomes difficult to diagnose as there is multiple systemic and nonspecific symptoms such as weakness, weight loss and fever. It can also affect other part of the like pleura, joints, pleura, and genitourinary system.

DRUG RESISTANCE[25,26]

The burden of the MDR-TB is increasing worldwide. Treatment of the multi drug resistance TB is challenging and has community health problem especially in developing countries. The present information from the various

drug resistance surveillance studies says that the cases of MDR-TB is less in our country if we compare with the other developing countries. Because of inadequate treatment of the MDR-TB the burden of drug resistance tuberculosis may rise and pose as a public health emergency. Clinical features of drug resistance TB is not much differs from the non drug resistance TB.

If the Tubercle bacilli is sensitive to low concentration of the drug in a uniform manner then it is called as “sensitive strains”. If the tubercle bacilli can grow in the higher concentration of drug it is called as resistant strain. In other means which can be explained as reduction of the sensitivity to the drug so that it can grow significantly in higher concentration of the drug (Dr.D.A.Mitchison 1961) and definitely shows different characteristics from that of wild strain which had never come in contact with the wild strain.

The definition of drug resistance of Mycobacterium tuberculosis was adopted by the international group of specialists assembled by the world Health Organization (WHO) in 1969. This definition was established by testing a large number of wild strains against three drugs available at the time and minimal inhibitory concentrations (MIC) of these drugs where established in starch Free Lowenstein Jensen (LJ) Medium. It was suggested that a strain would be considered resistant if one percent or more of the bacterial population was resistant to a designated concentration of drug. With monotheraphy like streptomucin alone or inadequate theraphy the number of sensitive bacilli decreased while the resistant bacilli increased in lung cavities of the tubercular patient, this has been called the “Fall and Rise” phenomenon.

Table.3

OPERATIONAL CAUSES WHICH HELP IN THE EMERGENCE OF THE DRUG RESISTANCE IN TUBERCULOSIS

(RNTCP GUIDELINES 2010)[16]

Inadequate regiments: Providers/Programmes:-

1) Absence of guidelines or poor guidelines
2) Not following the guidelines
3) Shortage training to staff
4) Treatment with out monitoring
5) Poor functioning or funding of programmes

Drugs: Inadequate supply/quality:-

1) Quality of the drug inadequate
2) Storage condition are Bad
3) Non-availability of some drugs
4) Incorrect dosagesand combination

Patients: inadequate drug intake – Poor adherence

1) No free drugs
2) Drug side effects
3) Lack of knowledge, information
4) Socio economic status
5) Malabsorption
6) Disorder of Substance abuse.

TERMINOLOGY OF DRUG RESISTANCE[25,26]

Drug resistance in Tuberculosis could be classified as

1. Primary

2.Acquired

3. Initial

4.Natural

Strain of Mycobacterium tuberculosis which has never had been exposed to any of the anti tubercular drug in the past is called as the wild strain.

1. **Primary Resistance**

If patient acquires resistant wild strain called as primary resistance. The development of the resistance is because of exposure to the drug itself, but in another patient who already had taken the anti tubercular treatment.

2. **Acquired Resistance**

Resistance towards the anti tubercular drug is developed during the course of the treatment, subsequently selecting out of resistant mutant bacilli.

3. **Initial Resistance**

Initial resistance is defined as the resistance in patients who give a history of never been taken any anti tubercular treatment in the past and it includes primary resistance and resistance to previous treatment but forgotten by the patient is unaware of treatment which he had received.

4. Natural Resistance

Natural resistance is that resistance in which have never come in contact with the drug such as Mycobacterium bovis resistance to Pyrazinamide, Mycobacterium tuberculosis resistance to Penicillin, Mycobacterium africanum resistance to Thiocetazone. Wild type resistance is the result of random mutation in naturally susceptible strain before any exposure to anti tuberculosis drugs.

MECHANISM OF DRUG RESISTANCE[24,27]

The drug resistance in M. tuberculosis occurs by random spontaneous mutations of bacterial chromosomes which occur at a continuously but very less frequency. This varies from drug to drug which are used in the tuberculosis treatment. The chance of mutation of drug resistance is directly proportional to the number of the bacteria. Conversion of resistant bacilli to isoniazid and streptomycin in mycobacterium tuberculosis occurs as a single step mutation. The mutations rates are very low for most of the drugs and the mutants resistance to one of the several anti tuberculosis drugs appear once in every 10^7 cells. Thus development of drug resistance is because of the pre-existing resistance mutants in the bacteria which already having.

In clinical practice combinations of two or more anti tuberculosis drugs are given to the patients in view of eliminating all mutants resistant to any of the drugs. The rates of spontaneous resistance are 1 in 1,000,000 organisms for Isoniazid, 1 in 1,000,000 for Rifampicin, and 1 in 1,000,000 for ethambutol and 1 in 1,000,000 for streptomycin. Assuming they are independent events the

chance of occurrences of resistance to more than one anti tubercular drug is the probabilities for each drug alone.

Bacterial population inside the cavity pulmonary lesion is estimated to be 1,000,000,000 organisms. So, bacterial populations of these lesions is likely to having a less number of mutants resistance to one of the single anti TB drug. In rare occurrence the population has significant number of mutants resistance to two or more drugs at the same time. Development of the drugs resistant tuberculosis happens when there is a substantial increase in ratio of the organism, are resistance to one or more anti TB drugs.

Secondary or acquired drug resistance happens when the less numbers of drug resistance mutants are selected, due to inadequate anti tuberculosis treatment. To develop secondary resistance it may take about 2 weeks but usually takes more than 2 weeks (one to four months) after the starting of anti tubercular drugs when the population of the tubercular bacilli is very high. Primary drug resistance happens when the patient with mycobacterium TB organism resistant to 1 or more drugs before the patient is treated with the drug in unanswerable.

Initial drug resistance is an entity which includes all primary drug resistance and also concealed acquired resistance. This sort of concealed acquired resistance will pose a major threat to the outcome of treatment. For example, the risk of relapse with isoniazid resistance organism increase by about 4% per month or prior therapy, but up to 23% of patients in one study treated for one month with isoniazid alone had isoniazid resistant organism.

PROPOSED THEORIES

Knowledge regarding the mechanism of the development of drug resistance to various anti tuberculosis drugs is very little. So many theories have been put forward to explain the mechanism of development of drug resistance in micro organisms, out of which following are relevant to mycobacteria:

1. Interference in uptake or penetration of the drug in to the bacterial cell.
2. Development of insusceptible metabolic pathways.
3. Destruction of drug.

Using the 14C labeled isoniazid Barclay et-al found that isonizid resistant strains take up markedly less radioactive material than the susceptible strains. Youatt et-al confirmed these findings and suggested that the possible reason could be due to alternation in cell permeability.

MULTI DRUG RESISTANT TUBERCLULOSIS (MDR TB)[24,25]

Definitions:

When mycobacterium tuberculosis is resistant for atleast Isoniazid (H) and Rifampicin (R) with or without resistance to other TB drugs used is called as MDR-TB.

IMPLICATIONS OF DRUG RESISTANCE

1. The most important implications of drug resistance (primary and / or acquired including MDR) is the outcome of the treatment. The response in patients with multi drug resistant organism is very bad both in immune competent and immunocompromised patients.

2. The second and equally important implication is the spread and transmission of drug resistant tuberculosis. This is much more dangerous than the previous implication. The seriousness of the spread of drug resistant tubercle bacilli is magnified several fold when patients involved are infected with HIV.

GLOBAL PREVALENCE OF DRUG RESISTANT TUBERCULOSIS[12,13]

Till now total world wide census of new Tuberculosis cases with MDR-TB is 3.4% (1.9%-5%) and it has been about 20% (14%-25%) of Re-treatment cases with MDR-TB.

PREVALANCE OF DRUG RESISTANCE IN INDIA[12,13]

Several surveys estimated 2.1% (1.5% - 2.7%) proportion of MDR-TB in New TB cases and 15% (13%-17%) proportion MDR-TB in treated previously cases. To compare with world wide rates, the proportion of MDR-TB is less in our country. According to WHO, TB Report 2010 TB, Multidrug and extensively drug-resistant TB (M/XDR-TB) – it has been estimated 99,000 MDR TB cases in India in 2008 (range 79,000 – 1,20,000) and sixty four thousands MDR-TB cases out of notified pulmonary TB cases in India according to 2011 report.

EXTENSIVELY DRUG RESISTANT TUBERCULOSIS (XDR – TB)[31]

XDR-TB is a subtype of MDR-TB which is resistance to second line drugs i.e. any fluoroquinolone and to at least one of the three second line injectable drugs (capreomycin, kanamycin and amikacin).Very few surveys suggested that no XDR in the new cases and the prevalence among retreatement is 0.5%.16.

DIAGNOSIS

Evaluation for starting the management will include the following:

1. History taking in detail

2. Measurement of Weight

3. Measurement of Height

4.CBC with ESR

5.Blood sugar to screening of Diabetes Mellitus

6.Liver Function Tests

7.Renal function test

8.Thyroid function test

9.Urine Complete

10.Pregnancy test(for all women- child bearing age group)

11.Chest X ray

12.Sputum for AFB, Sputum Culture and sensitivity

13.GENE XPERT/RIF[28]

13.HIV 1 & 2

Apart from routine blood investigations definite diagnosis of Pulmonary tuberculosis is confirmed by culturing of Mycobacterium Tuberculosis. (Flow Chart1). Sputum smears and cultures can be done for acid fast bacilli. Most preferred method for confirmation is fluorescence microscopy (fig.2.auromine-rhodamine staining) which is confirmative than conventional Ziehl-Neelsen

staining. This Ziehl-neelsen staining most widely used in india for confirmation of Pulmonary tuberculosis.

RADIOLOGICAL INVESTIGATIONS

Chest X ray and CT chest will be useful in a active pulmonary Tb which may shows infiltrates or consolidations with or without cavities are commonly seen in the upper segment, with or without mediastinal or hilar lymphnode enlargements or pleural effusions. The above lesions are may be appear anywhere in the lung fields. And in disseminated TB there were many tiny nodules seen throughout the lung fields is seen - the so this is called as miliary TB. In HIV and other immunocompromised persons, any abnormality may indicate TB or the chest X-ray may appear normal. Abnormalities are seen in the CXR may be suggestive, but this is not give diagnostis of Pulmonary TB definitely. In chest radiographs are used for rules out of the possibility of pulmonary TB in a person for positive tuberculin skin test with out symptoms of the disease.

Flow Chart 1

Flow chart 1: Diagnostic algorithm for pulmonary tuberculosis

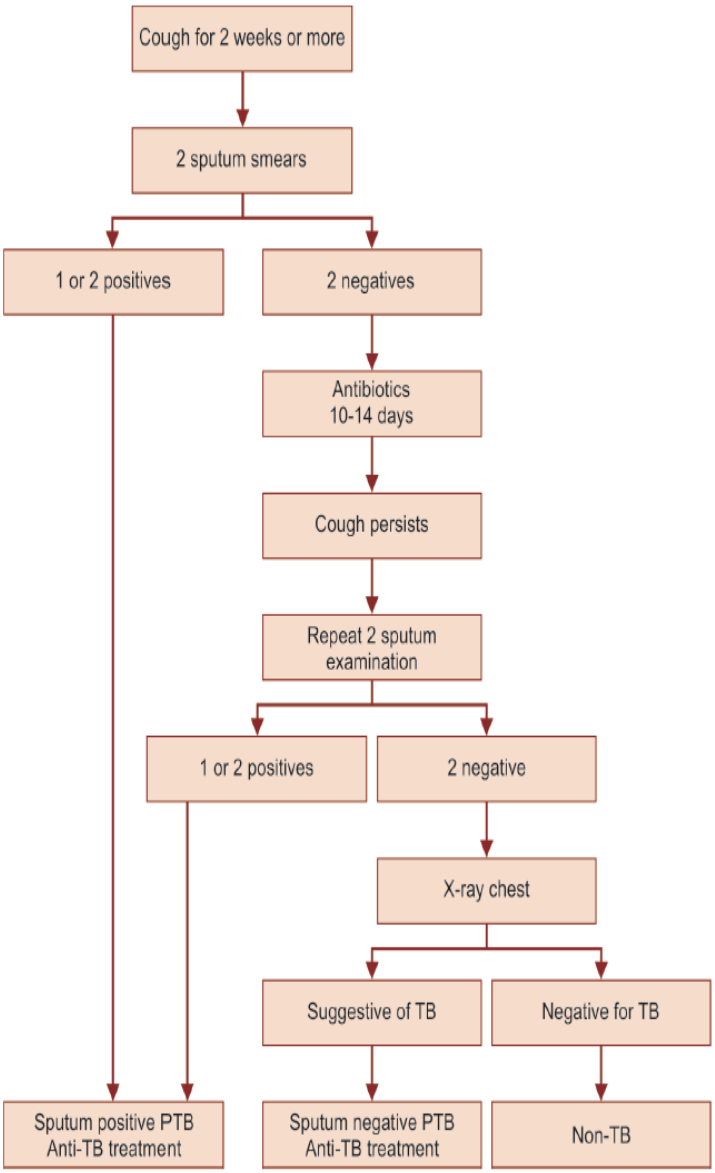
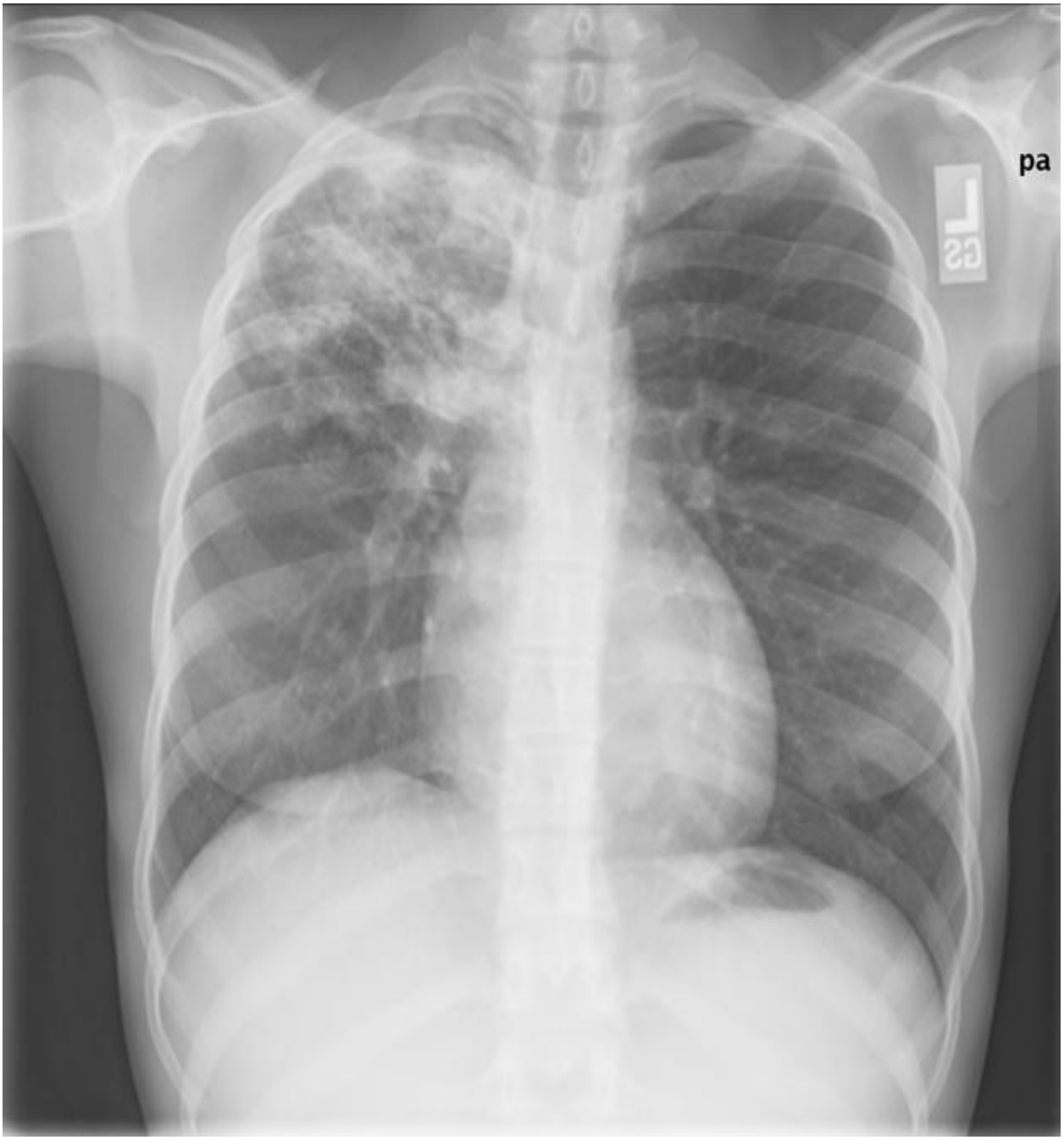


Figure 3



The following Diagnosis Technologies are currently available in India under RNTCP and also Recommended for the Diagnosis of MDR-TB[32]:

MDR-TB diagnostic technology	Choice
Molecular DST [e.g. cartridge-based automated nucleic acid amplification test (CBNAAT) or line probe assay (LPA)]	First
Liquid culture isolation and LPA DST	Second
Solid culture isolation and LPA DST	Third
Liquid culture isolation and Liquid DST	Fourth
Solid culture isolation and DST	Fifth

Abbreviations: MDR-TB, Multidrug resistant tuberculosis; DST, Drug susceptibility testing

GENEXPERT/RIF[28]

The GeneXpert MTB/RIF is the new test that is very helpful in diagnosing tuberculosis (TB) by identification of Mycobacterium Tuberculosis.This test is identify Mycobacterium tuberculosis and also drug resistance to Rifampicin (RIF) with in 2 hours. Compared to the standard cultures which takes two to six weeks for MTB to grow and the conventional drug resistance tests will take nine to ten weeks. The results by the Xpert MTB/RIF assay used in selecting treatment regimens and control of TB are as soos as possible.

This is a cartridge-based fully automated CB-NAAT (Catridge-Based Nucleic Acid Amplification Test) for TB identification and rifampicin drug

resistance testing. This instrument purifies, concentrates, amplifies (by a rapid and real-time PCR) and identified targeted nucleic acid sequences in the TB genome, and gives the results from the sputum samples within 2 hours, with minimal time. Even though the molecular amplify technology is the proven technique for TB diagnosis, other available test methods are difficult and having constraint for routine. The need for sample processing and DNA extraction adds another level of complexity to implementation in settings where resources are limited.

GeneXpert was launched by Cepheid (Figure.4) in 2004 and simplified molecular testing by fully integrated and automated the three stages of processes

1.Sample preparation,

2.Amplification

3.Detection.

The stages are above for real-time PCR-based molecular testing. The Xpert MTB/RIF test the only molecular test available and useing a cartridge contains all the required increments necessary for the reaction, which includes the lyophilized reagents, liquid buffers and the wash solutions. Target detection and characterization is performed in real time using a six-colour laser detection device.

Advantages of the Xpert MTB/RIF Assay

Main advantages of Xpert MTB/RIF assay are

1. Results are arrives in a short period of time

2. Very less training is required for testing.

3. And further more that the Xpert MTB/RIF will fastly identifying the multidrug-resistant TB (MDR TB).RIF resistance is the main indictor of MDR TB because the resistance to RIF mostly combined with the resistance for Isoniazid.
4. Accurate and diagnosis of RIF resistance gives to start treatment effectively for MDR TB patients earlier than any other drug susceptibility testing.
5. Those who are NOT having TB disease, fast and quick results gives, cost effective by avoiding unnecessary stay in the hospital.

Disadvantages

1.This instrument needs power supply which should be stable, continuous and uninterrupted and should be connected to a computer system for analysis of data.
2. This instrument needs calibration every year, which should performed by a trained technician using specialized calibration equipment.
3.GeneXpert device (GX4) are most commonly used and having a limited testing capacity, and bigger systems (or linked devices), if we do more cost which causes more expenditure.

Interpretation of results

GeneXpert MTB/RIF should be transcribe along with clinical, CXR, and other lab reports. This assay should not replace the sputum smear for acid-fast bacilli, culture , and drug susceptibility testing in growth, genotyping to be done for identification of outbreaks.

Results from this assay gives MTB was found in the sample or not. Sometimes , the result is “invalid " hence it must be repeated. If the MTB was found, the results gives as follows,

1.Detected,

2.Not detected

3.Indeterminate.

Regardless of the result, the patients specimens mycobacterial culture should be done to confirm isolates for drug susceptibility testing and genotyping.

RIF Resistance Detected

If the it comes as positive for MTB and for RIF resistance, it means the bacteria having a possibility of resistance to RIF. It has to be confirmed by another rapid testing. If the RIF resistance is reconfirms, the rapid molecular tests for drug resistance for the both first-line and second-line drugs should be done, so an appropriate drug regimen will be selected and started.

RIF Resistance Not Detected

Results came as positive for MTB, Not for RIF resistance mean, so the bacteria are possibly susceptible to RIF. It should undergone growth-based susceptibility testing to first-line TB drugs.

RIF Resistance Indeterminate

If the Results are positive for MTB and indeterminate for RIF resistance means, the test inconclusive for resistant to RIF. Then the Growth-based susceptibility testing to first-line TB drugs has to be done.

Figure 4

TREATMENT OF TUBERCULOSIS UNDER RNTCP[16]

The mainstay of treatment for to ensuring the high cure rates, to prevents the drug resistance, to reduces the relapse rates and to avoid the transmission of the TB in community by early detection and management.

Table 4

TREATMENT CATEGORIES UNDER RNTCP[32]

TREATMENT GROUPS	**TYPE OF PATIENT**	**REGIMEN**	
		INTENSIVE PHASE	CONTINUATION PHASE
CAT I (NEW*)	Sputum smear-positive Sputum smear-negative Extra-pulmonary Others	2 H3R3Z3E3	4 H3R3
CAT II (Treated **)	Smear- positive relapse Smear-positive failure Smear-positive treatment after defaukt Others	2 H3R3Z3E3S3 / 1H3R3Z3E3	` 5H3R3E3

*CATEGORY I New includes former categories I and III

**CATEGORY II Previously Treated (Formerly Category II)

The prefixed number suggested the total number of months of treatment. The subscript which is mentioned after the letters refers to the number of doses per week.

The dosages for drugs are as follows for adult more than 50kgs.

ISONIAZID (H) 600mg

RIFAMPICIN (R) 450mg

PYRAZINAMIDE (Z) 1500mg

ETHAMBUTOL (E) 1200mg

STREPTOMYCIN (S) 750mg

DOTS-Plus[16,17]

DOTS-Plus refers to DOTS programmes that add components for MDR-TB diagnosis, management and treatment under RNTCP. Management of the MDR-TB is very crucial and difficult as well. Management of MDR-TB needs selected institutions with good experience, experts availability and availability of required diagnosis and management facilities.

The following are the criteria to say patient is MDR-TB suspect.

(indications for MDR-TB diagnosis)

1) A new smear +ve patient remaining smear+ve at the end of 4th month.
2) A new smear –ve patient becoming smear-positive at the end of 4th month.
3) A patient treated with regimen for previously, treated remaining +ve at fourth month.
4) Smear+ve contacts of an established/confirmed MDR-TB case.

RNTCP Regimen for MDR-TB[16,17]:

This regimen contains of 6 drugs Kanamycin, Levofloxacin, Ethionamide, Pyrazinamide. Ethambutol, and Cycloderine during 6-9 months if

Intensive phase and 4 drugs – Levofloxacin, Ethionamide, Ethambutol and Cycloserine during the 18 months of the continuation phase. And Substitute or reserve drugs are Para amino salicylic acid, Moxifloxacin and Capreomycin.

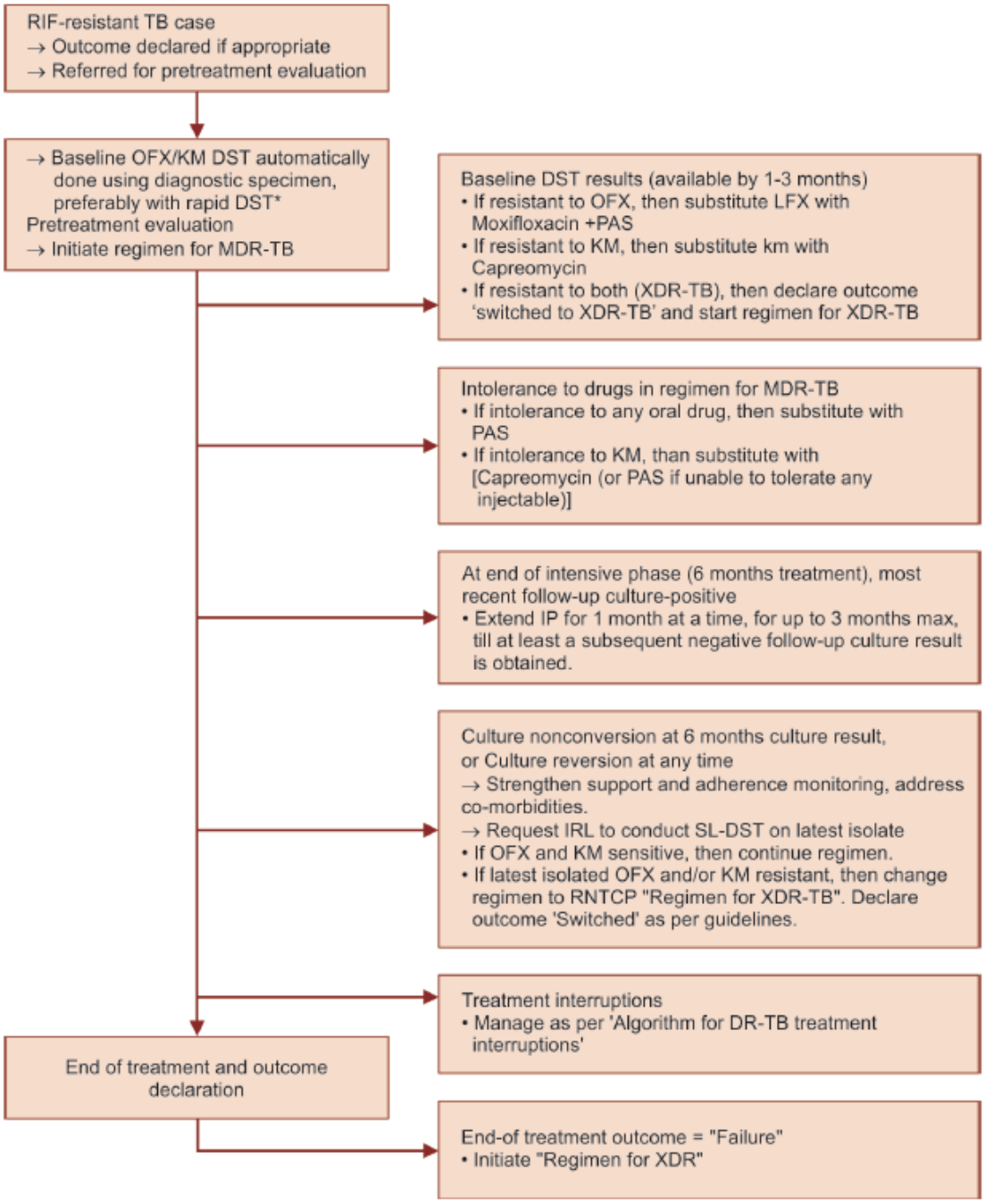
Above regimen can be adjusted for special situations as follows:

- If no tolerance to Inj. Kanamycin, then Capreomycin (or PAS can be used if injectable not feasible) is the subsititute drug.
- If the intolerance leads to topping of other oral second line drug, PAS is available substitute drug.
- Mono- resistance of kanamycin substitute with Capreomycin.
- Mono-resistance of Ofloxacin should altered with substitution of Levofloxacin with the combination of Moxifloxacin and PAS
- Baseline ofloxacin and Kanamycin resistance should evaluated for XDR TB.

Regimen for XDR TB[16,17]:

All XDR TB patients should undergo full pre-treatment evaluation afresh, and also includes consult with thoracic surgeon for consideration of surgery. MDR TB patients diagnosed as XDR TB may gives as outcome of Switched to "Regimen for XDR TB". The decision and initiation of regimen for XDR TB is to be taken by the concerned DR-TB Centre Committee(Flow chart 2.).

Flow chart 2: Integrated treatment algorithm



Intensive Phase: (6 to 12 months)

Consists of 7 drugs – Capreomycin(CM), PAS, Moxifloxacin(Mfx), High dose-INH, Clofazamine, LInezolid and Amoxyclac

Continuation Phase (18 months):

Consists of 6 drugs- PAS, Moxifloxacin, High dose INH, Clofazamine, Linezolid and Amoxyclav. The dosages of drugs are vary according to weight of the patients. All drugs should be given by daily basis. Inj.Capreomycin will be given for 6days/week. Reserve and substitute drugs are Clarithromycin(Clr), Thioacetazone (Thz).

These are can be used in the following conditions:

- If patient is on PAS , PAS can be replaced with one of the drugs in reserve in the regimen for XDR TB.
- Intolerability for one or more drugs
- If culture shows resistance to capreomycin.

The change from Intensive Phase to Continuation Phase should be done only after culture reports i.e. Two Continuous negative cultures should be taken at least one month apart. If there is delay in culture conversion, the Intensive Phase can be extended from six months up to a maximum of 12 months.

FIRST LINE DRUGS[16,17,32]:

ISONIAZID (H)

It is an essential component of all anti tubercular regimen, unless patient is not able to tolerate or bacilli are resistant. It is tuberculocidal. It acts on extracellular as well as intracellular as well as intracellular bacilli and equally effective in acidic and alkaline medium.

It acts by inhibition of mycolic acid synthesis (unique fatty acid component of mycobacterial cell wall). A gene labeled inh A encodes for a fatty syntzyme is the likely target of INH action. The sensitive mycobacteria concentrate INH and convert it by a catalase peroxiase enzyme into an active metabolite that appears to interact with the inh A gene.

The most common mechanism of INH resistance is by mutationat of catalyse – peroxidase gene so that bacilli do not generate active metabolite of INH. INH resistance may also involve mutation in the target inh A gene. The incidence of INH resistance varies widely among different populations. Combined with other drugs, INH has good resistance preventing action and no cross resistance with other anti tubercular drugs occurs. It is completely absorbed orally and penetrates all body tissues. It is extensively metabolized in liver, mostly by acetylation. Dose:10 mg/kg, max 600 mg.

INH is well tolerated by most patients. Due to interference with utilization of pyridoxine and excretion in urine it leads to peripheral neuritis. Pyridoxine given prophylactically (10 mg/kg) prevents neurotoxicity. INH neurotoxicity is treated by pyridoxine 100 mg/day.

Hepatitis, a major adverse effect of INH is more common in elderly, alcoholics, rare in children. It is dose relate and is reversible on stopping the drug.

RIFAMPICIN:(R)

It is a semi-synthetic derivative of rifamycin B obtained from Streptomyces mediterranei. It is bactericidal. The bactericidal action covers all sub populations of TB bacilli, but acts best on slowly or intermittently dividing bacilli. It acts on both extra and intracellular organisms. It acts by inhibiting DNA dependent RNA synthesis. Mycobacteria develop resistance to rifampin rapidly; however the incidence of resistance is less. Rifampicin resistance is always due to mutation in repoB gene (target of Rifampicin action) and reducing its affinity for the drug.

It is well absorbed orally and widely distributed in the body. It is metabolized in liver to an active deacetylated metabolite and excerted in bile.tl/2 is 2-5 hrs.

Rifampin is a microsomal enzyme inducer- enhances its own metabolism as wel as that os many drugs including OCP, warfarin, steroids, ketaconazole, etc…Hepatitis is a major adverse effect and is dose related. It occurs in patients with preexisting liver disease. Other serious but rare reactions are breathlessness, purpura, haemolysis, shock, renal failure. Minor reactions not requiring drug withdrawal are rash, flushing, chills, fever, headache, nausea, and vomiting, abdominal cramps with or without diarrhea. Urine and secretions may become orange red but this is harmless.

It may also be used in leprosy, prophylaxis for meningococcal and H.influenzae meningitis, 2nd choice in MRSA, Diptheroid and legionella infections. It can be used in brucellosis in combination with doxycycline. DOSE:10 mg/kg max: 600mg

ETHAMBUTOL: (E)

It is selectively tuberculostatic. Fast multiplying bacilli are most susceptible. It has been found to hasten the rate of sputum conversion.

It acts by inhibiting arabinogalactan synthesis and thereby to interface with mycolic acid incorporation in mycobacterial cell wall. Resistance to this develops slowly. No cross resistance with any other anti tubercular drugs.

It is distributed widely but penetration of meanings is incomplete. It is temporarily stored in RBC. It excreted in urine. t ½ is 4 hrs.

It has very few side effects, so patient acceptability is good. Optic neuritis is the most common side effect. Loss of visual acuity/ color vision will be there and it is reversible on stopping the drug, (dose and duration dependent). Other side effects are rashes, fever, nausea, hyperiricemia. DOSE : 15mg/kg/day.

PYRIZINAMIDE : (Z)

Pyrizinamide is weakly tuberculocidal but more active in acidic medium. It is more lethal to intracellular as well as bacilli at site of inflammation. It is highly active during the first 2 months of therapy when inflammatory changes are present.

It also acts by inhibiting mycolic acid synthesis, ut by interacting with a different fatty acid synthase gene, resistance to this drug develops very rapidly

and is due to mutation in the gene which encodes for the enzyme generating the active metabolite of pyrizinamide.

It is absorbed orally, widely distributed, good penetration in CSF. It is extensively metabolosed in liver and excreted in urine. plasma t ½ is 6-10 hrs. Hepatotoxicity is the major side effect,Hence it contraindicated in liver cell failure. Otherside effects are arthralgia,flushing,fever.

DOSAGE: 1.5 gm/day with a maximum of 2 gms

STREPTOMYCIN(S):

It was the first clinically used anti TB drug. It is tuberculocidal. It acts only on extracellular bacilli. It has poor penetration into the cells. It is highly ionized. It is neither absorbed nor destroyed in GIT. It is not metabolized – excreted unchanged in urine. t ½ is 2-4 hrs. half life is prolonged in patients with renal failure, elderly, neonates.

It is an aminoglycoside. It acts by inhibiting protein synthesis. It is more active in alkaline medium.

Resistance develops by the following mechanism

- Mutation or by acquisition of plasmid which encodes for inactivating enzymes.
- Mutation decreasing the affinity of ribosomal proteins that normally bind streptomycin.
- Decreased efficiency of the drug transport mechanism.

It has the lowest nephrotoxicity among the aminoglycosides. It produces ototoxicity. Rashes, fever, eosinophilia, exfoliative dermatitis can occur. Pain at IM site is common. DOSE: 0.75 – 1.0 gm daily.

It is used in plague, tularemia and SABE other than tuberculosis.

SECOND LINE DRUGS[16,17,32]:

ETHIONAMIDE (Eth):

It is tuberculostatic. It has same mechanism of action of INH. It acts both on intra and extracellular organism. Resistance to this drug develops rapidly. It is absorbed orally and distributed widely including CSF. It is completely metabolized and has a short duration of action, t ½ is 2 – 3 hr.

The recommended dose is 1 gm/day, but more than 0.5 gm is not tolerated by most patients because of anorexia, nausea, vomiting and abdominal discomfort. Other side effects are aches and pains, rashes, hepatitis, peripheral or optic neuritis, mental disturbances and importance. It is seldom used ; only in cases of resistance to better tolerated drugs.

CYCLOSERINE:

It is antibiotic obtained from S.orchidaceus. it is a chemical analogue of D-Alanine.

It inhibits cell wall systhesis by inhibiting the enzymes which recemize L – alanine and link two D – alanine residues.

It is tuberculostatic. Resistance to this drug develops slowly. No cross resistance seen. It is absorbed orally, diffuses all over, concentration in CSF is equal to that of plasma. About 1/3 metabolized, rest excreted unchanged in urine. CNS toxicity is high – sleepiness, headache, trenor, psychosis; convulsions maybe prevented by pyridoxine 100mg q 12hrly.

KANAMYCIN, AMIKACIN, CAPREOMYCIN:

These drugs may be used in place of streptomycin when necessary. MTB strains that are resistant to streptomycin may be susceptible to these other agents. They are bactericidal by disrupting bacterial protein synthesis. They are available only in the parenteral form. All are excreted unchanged by the kidney. All are given a a dose of 0.75 – 1.0 gm im / day. All exhibit similar ototoxic and nephrotoxicity, they are not combined among themselves or with streptomycin, it is nowadays used in the treatment for MDR – TB.

QUINOLONES:

The fluoroquinolones are a useful new addition to the anti tubercular drugs. Ciprofloxacin, ofloxacin, moxifloxacin and sparfloxacin are active against M.tuberculosis as well as M.avium complex and M.fortuitum. because of their good tolerability, they are being increasingly used in combination regimens against MDR TB and MAC infection in HIV patients.

They disrupt the bacterial chromosome by inhibiting the super coiling action of DNA gyrase.

DOSE: Ciprofloxacin: 750 mg BD

Ofloxacin : 800 mg OD

Levofloxacin : 500 mg/day.

Side effects are abdominal discomfort, insomnia, and photosensitivity.

They are not advisable to be used in pregnancy and children because of fear of arhtropathy. Resistance to these drugs develops because of several single gene mutations in DNA gyrase subunit.

PARA-AMINO SALICYLIC ACID:(PAS)

PAS is tuberculostatic. It is one of the least active drugs. It acts by inhibiting the folic acid pathway. It is well absorbed. Its penetration is good in all tissues except in CSF. This drug metabolized in liver. It may be given as single drug.T1/2 is 1 Hr.

Hepatotoxicity, hematological derangements and inhibition of prothrombin synthesis have been reported.

DOSE: 8-12 gm/day.

RIFABUTIN

It is structurally similar to Rifampicin and it also acts by inhibiting DNA dependent RNA polymerase in bacteria. It is more lipid soluble, hence it has longer half life. They do not interfere with pharmacokinetics of protease inhibitors, so it can be used with ART drugs.

DOSE: 300mg/day

Side effects includes polyartharlgias, arthritis, skin hyperpigmentation, leucopenia can be minimized by reducing the dose.

CLOFAZAMINE:

It is bacteriostatic, liphophilic agents that bind to mycobacterial DNA. It is commonly used in the treatment of non tuberculous mycobacterial infections.

DOSE : 300mg/day.

MATERIALS AND METHODS

SOURCE OF STUDY:

Data consists of primary data collected by the principal investigator directly from the patients who are admitted in the Government Medical College and Hospital.

DESIGN OF STUDY: Cross Sectional Study.

PERIOD OF STUDY: One year, July 2014 - June 2015.
SAMPLE SIZE: 100

INCLUSION CRETERIA:

1. Patients (Both Genders) diagnosed 100 numbers of new smear positive pulmonary tuberculosis patients at Coimbatore Medical College Hospital.
2. Age above 18 yrs.

EXCLUSION CRITERIA:

1. Presence of secondary immunodeficiency states- HIV,
2. Diabetes Mellitus
3. Cancer patients,
4. Patients on corticosteroids or cytotoxic drugs
5. Extra pulmonary TB
6. Pregnancy and lactation
7. Patients not capable of giving consent (psychiatric patients).
8. Patients not willing to participate in the study (who refused to consent)

METHODOLOGY

The study is will be undertaken on the patients attending medicine outpatient department and admitted in the Coimbatore Medical College and Hospital, Coimbatore during the study period (July 2014 to June 2014). A total of 100 patients of new smear positive pulmonary tuberculosis will be included in the study.

The list of the patients enrolled in the study is appended along with the dissertation. The study excludes minors, pregnant women, mentally-ill and non-volunteering patients, Presence of secondary immunodeficiency states- HIV, Diabetes, cancer patients, patients on corticosteroids or cytotoxic drugs, Extra pulmonary TB, Pregnancy and lactation, Hepatitis B or C infections.

The study is proposed to be conducted after obtaining informed signed consent from the patients. The duration of the study is one year from July 2014 to June 2015. The principal investigator, after obtaining informed signed consent from the patients to participate in the study, collects their baseline characteristic details, medical history details and physical examination details.

The clinical history includes all risk factors like close contact with known MDR-TB or with person who died of TB/ failed treatment, failure to improve on current TB treatment and association with HIV or other immuno suppressions.

Diagnosis of TB will be confirmed as per Revised National Tuberculosis Control Programme (RNTCP) guidelines.

Sputum or gastric lavage of all cases will be sent for Culture and Drug susceptibility test (DST).

DST will be done by detection of drug resistant gene for Rifampicin by Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) [GeneXpert] at the Culture and Drug Susceptibility Testing Laboratory, Department of Thoracic Medicine, Coimbatore Medical College Hospital. Coimbatore.

INVESTIGATIONS:

1. CompleteHaemogram

2. ESR

3. RBS,B.Urea,S.creatinine

4. Liver function Test

5. Urine Complete

6. Chest X Ray

7. HIV Test 1&2

8. CB-NAAT (GeneXpert)

ANALYSIS OF RESULTS

TABLE 5.

DISTRIBUTION OF AGE

AGE in yrs	Frequency	Percent
<10	1	1.0
11 to 20	6	6.0
21-30	17	17.0
31-40	23	23.0
41-50	25	25.0
51-60	14	14.0
61-70	11	11.0
>70	3	3.0
Total	**100**	**100.0**

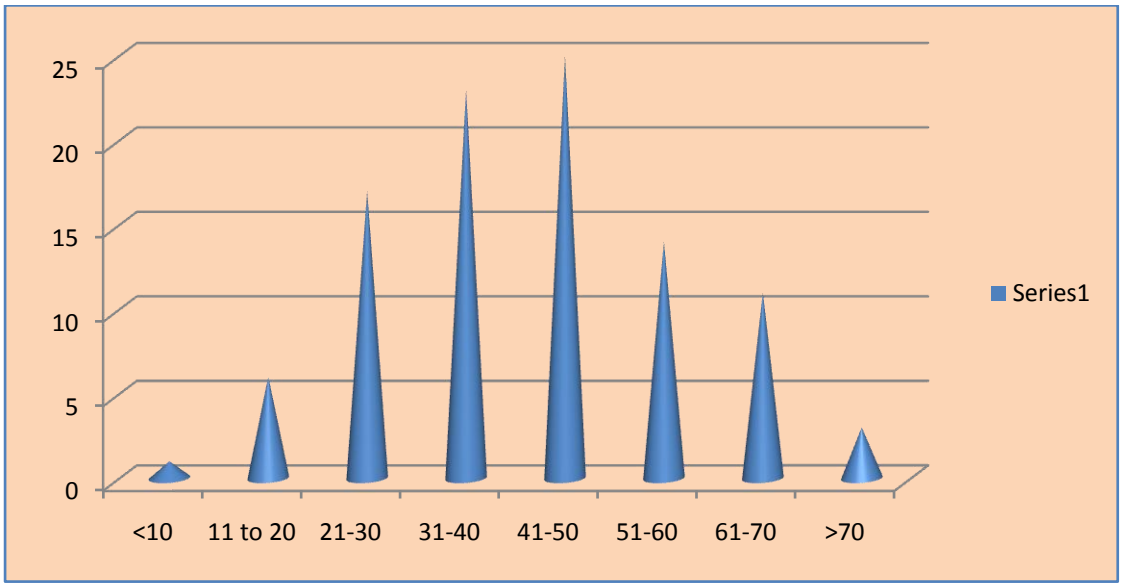


TABLE 6

DISTRIBUTION OF SEX

SEX	Frequency	Percentage
Female	16	16.0
Male	84	84.0
Total	100	100.0

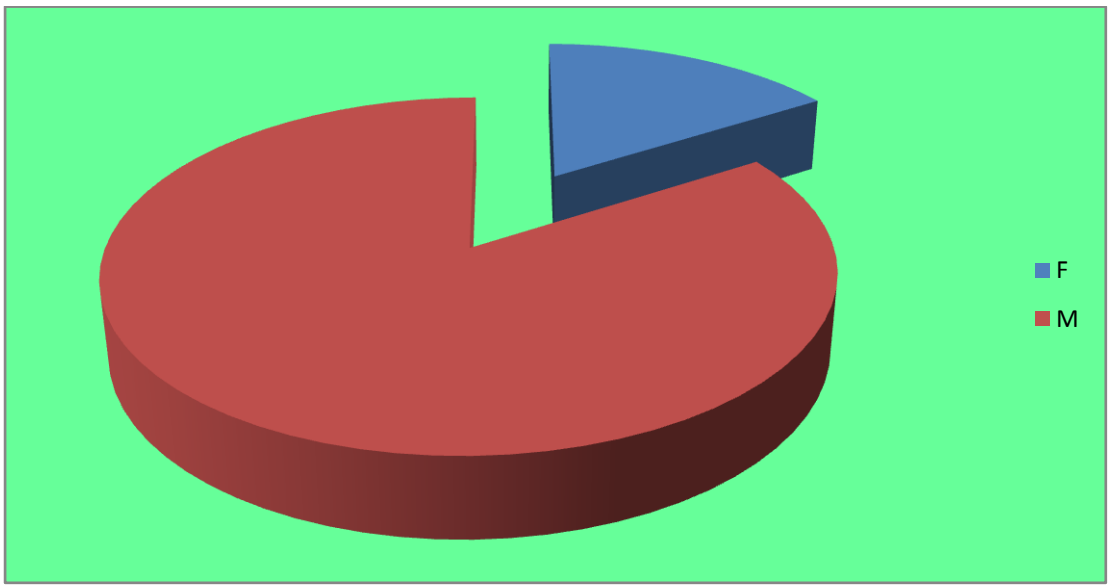
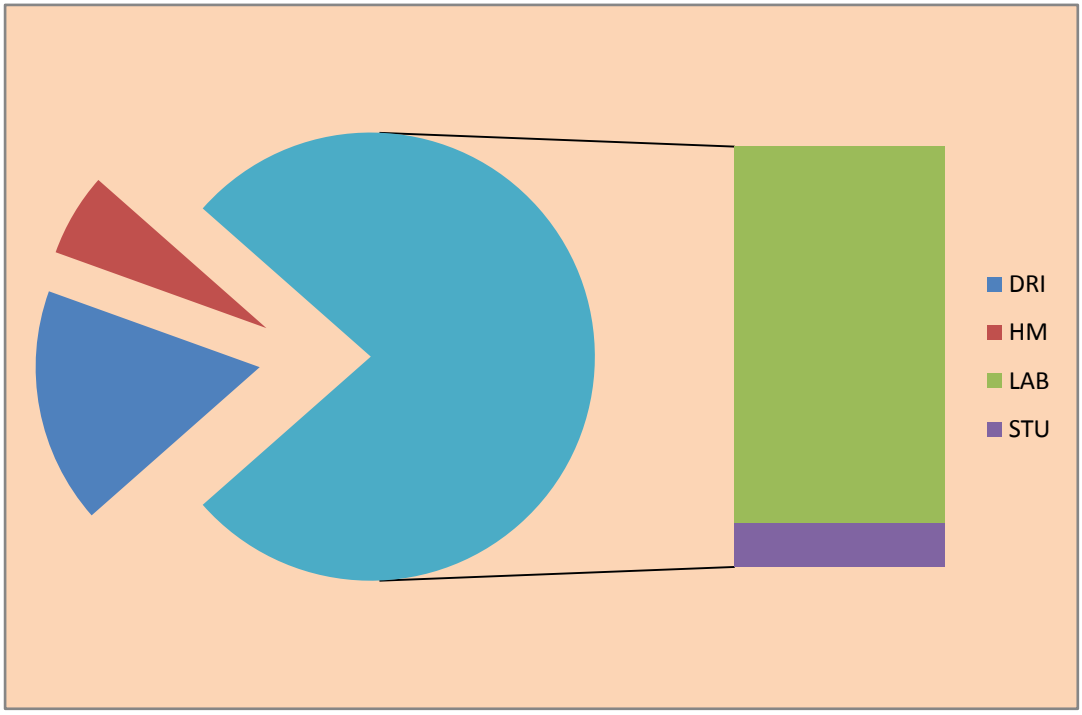


TABLE 7

DISTRIBUTION OF OCCUPATION

Occupation	Frequency	Percentage
DRIVER	17	17.0
HOME MAKER	6	6.0
LABOURER	69	69.0
STUDENT	8	8.0
Total	100	100.0



1. Total number of patients studied were 100.

2. Out of 100 patients Male patients were 84 and female patients were 16 in numbers.

3. Most number of patients were in the age group 41-50 followed by 31-40.

4.Total number of patients in the age group 41-50 were 25 (25%)

5. 69% of patients were Laborers, 17% of patients are drivers,8% of patients were students and 6% were Home makers

TABLE.8.

DISTRIBUTION OF COUGH

Cough	Frequency	Percentage
YES	100	100.0

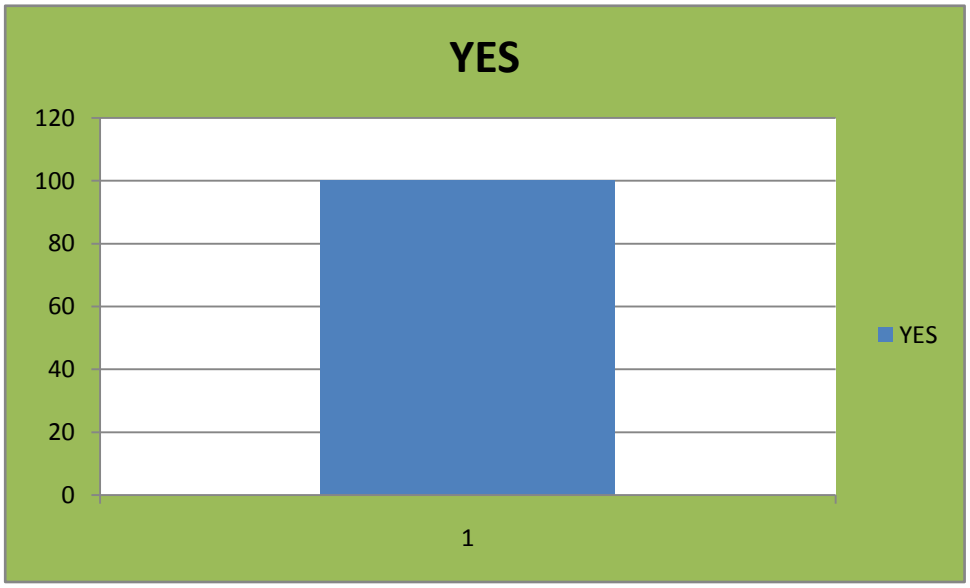


TABLE .9

DISTRIBUTION OF COUGH EXPECTORATION

Cough with Expectoration	Frequency	Percent
NO	7	7.0
YES	93	93.0
Total	100	100.0

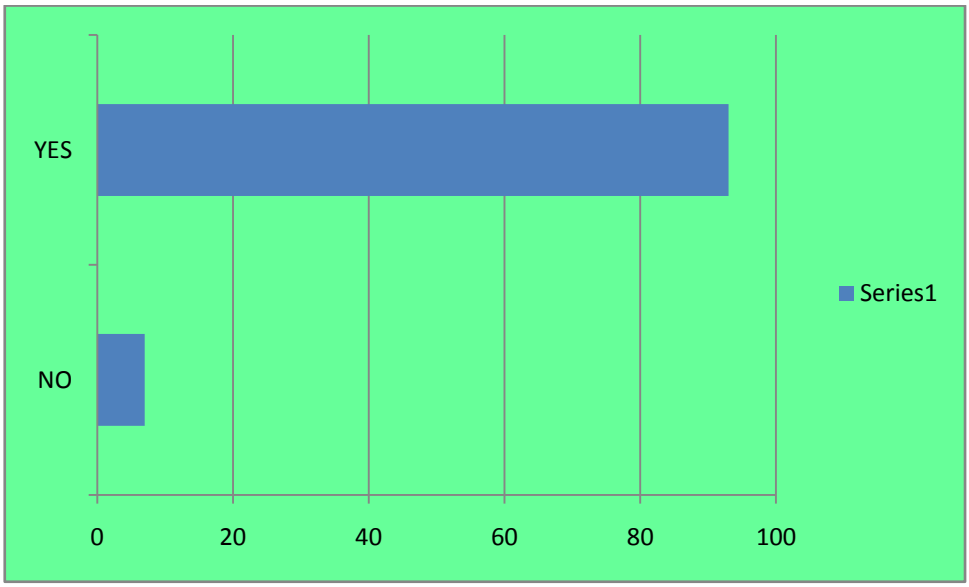


TABLE.10

DISTRIBUTION OF HAEMOPTYSIS

Haemoptysis	Frequency	Percentage
NO	66	66.0
YES	34	34.0
Total	100	100.0

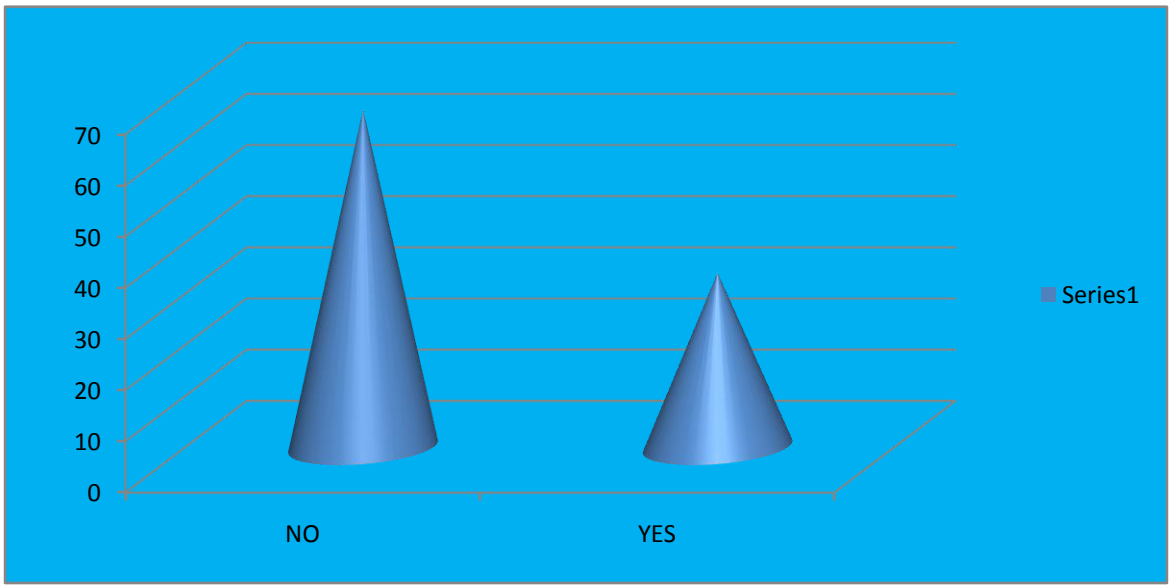
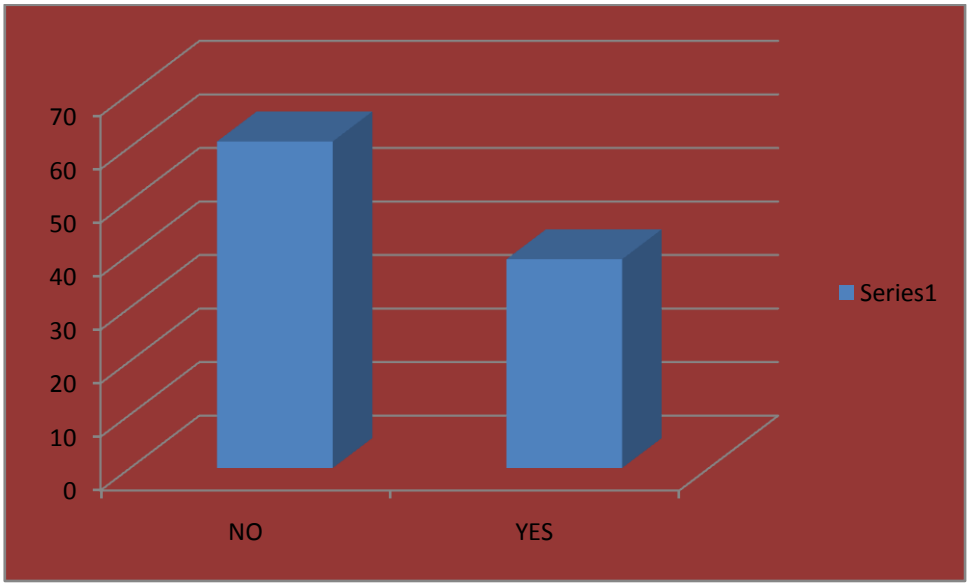


TABLE.11.

DISTRIBUTION OF FEVER

Fever	Frequency	Percentage
NO	61	61.0
YES	39	39.0
Total	100	100.0



1. All patients were having Cough(100%)

2. 93% of the patients were having Cough with Expectoration

3. 34% of the patients were having Haemoptysis

4. 39% of the patients were having fever

5. Most Common symptom with which patients were presented with Cough (100%) followed by expectoration (93%).

TABLE NO.12.

DISTRIBUTION OF PALLOR IN GENERAL EXAMINATION

Pallor	Frequency	Percent
NO	33	33.0
YES	67	67.0
Total	100	100.0

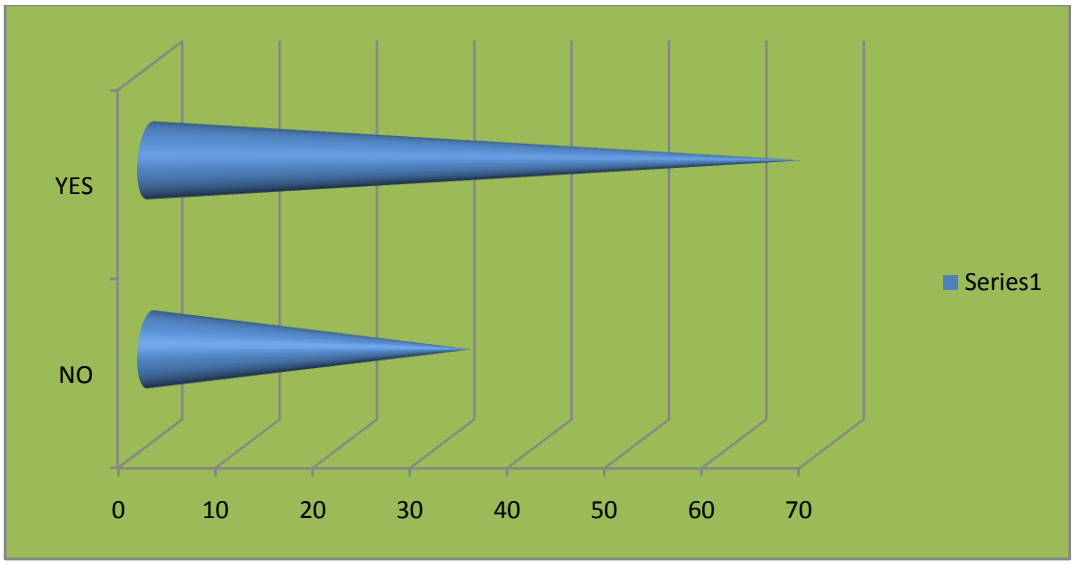


TABLE.13.

DISTRIBUTION OF THE POOR NUTRITION

Poor Nutrition	Frequency	Percent
NO	86	86.0
YES	14	14.0
Total	100	100.0

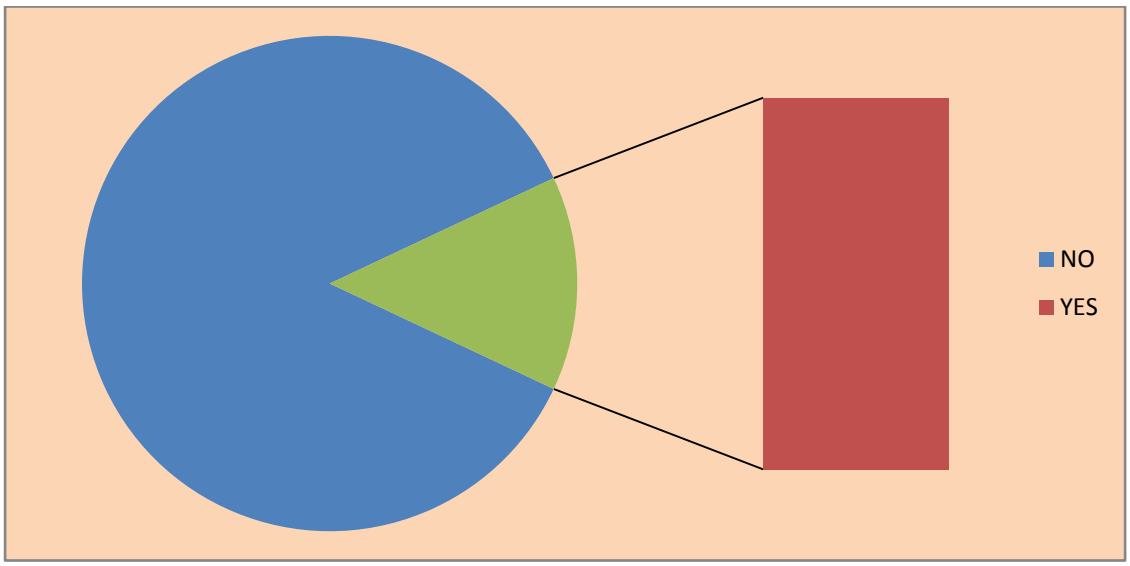


TABLE.14.

DISTRIBUTION OF CREPITATIONS (RESPIRATORY FINDING)

Crepitations	Frequency	Percent
NO	31	31.0
YES	69	69.0
Total	100	100.0

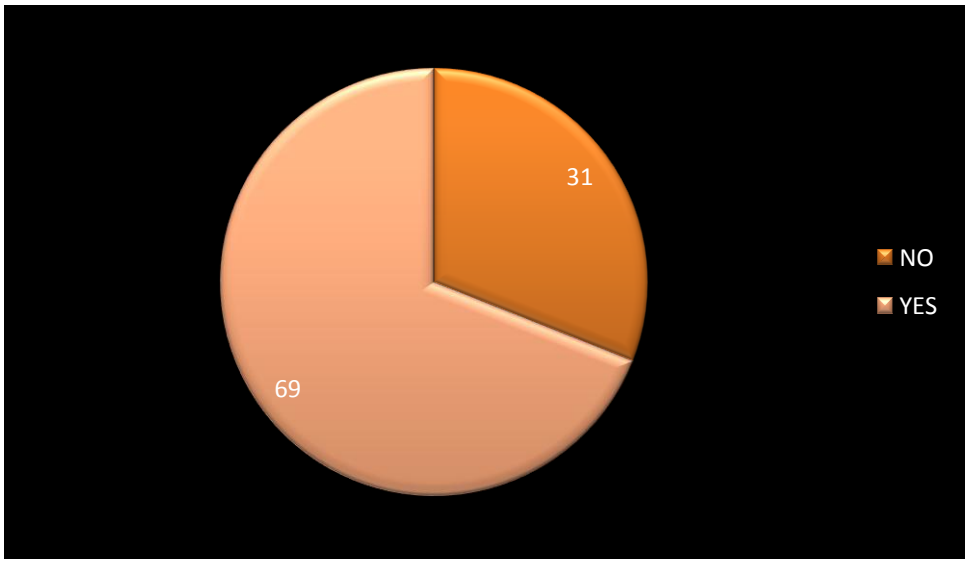


TABLE.15.

DISTRIBUTION OF WHEEZE

Wheeze	Frequency	Percent
NO	73	73.0
YES	27	27.0
Total	100	100.0

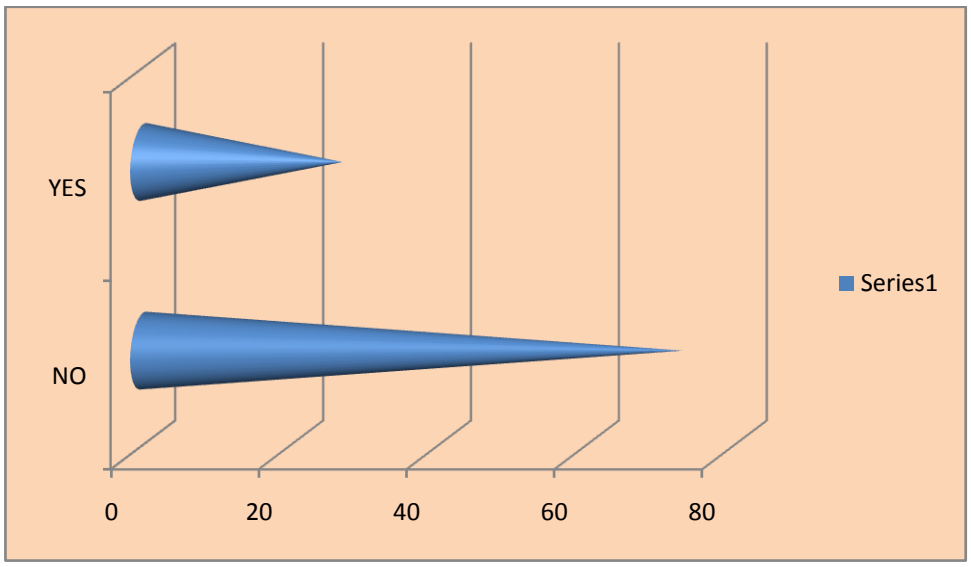
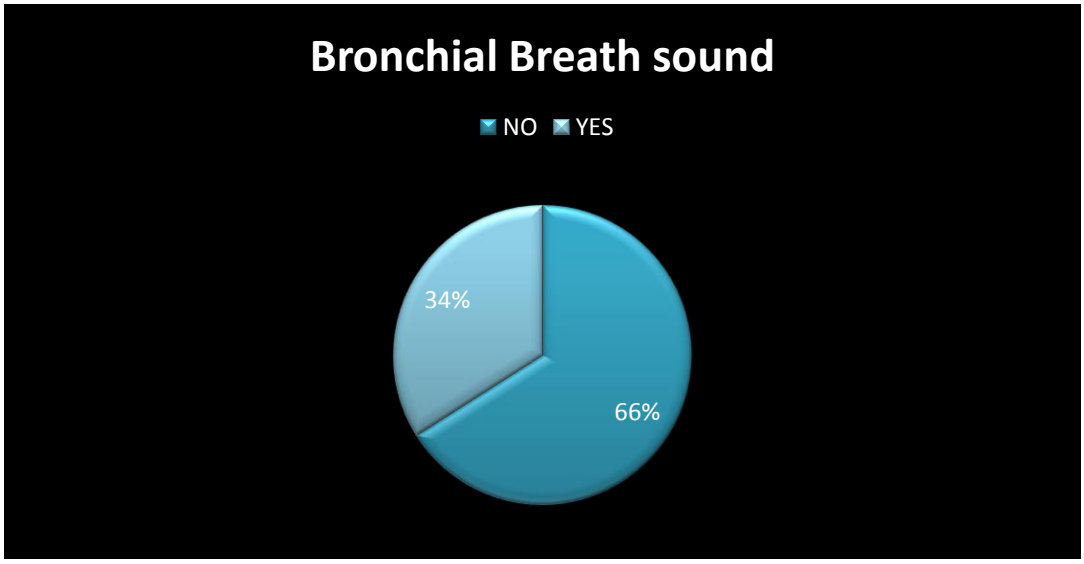


TABLE.16.

DISTRIBUTION OF BRONCHIAL BREATH SOUNDS

Bronchial Breath Sounds	Frequency	Percent
NO	66	66.0
YES	34	34.0
Total	100	100.0



1. 67% patients were looking pallor in General examination
2. 14% patients were with Poor nutrition in General examination
3. 69 % patients were presented with crepitations
4. 27% patients were presented with wheeze
5. 34 % patients were presented with Bronchial breath sounds
6. Most common sign presented in examination were crepitations followed by bronchial breath sounds

TABLE.17.

DISTRIBUTION OF ANAEMIA

Anaemia	Frequency	Percent
YES	27	27.0
NO	73	72.0
Total	100	100.0

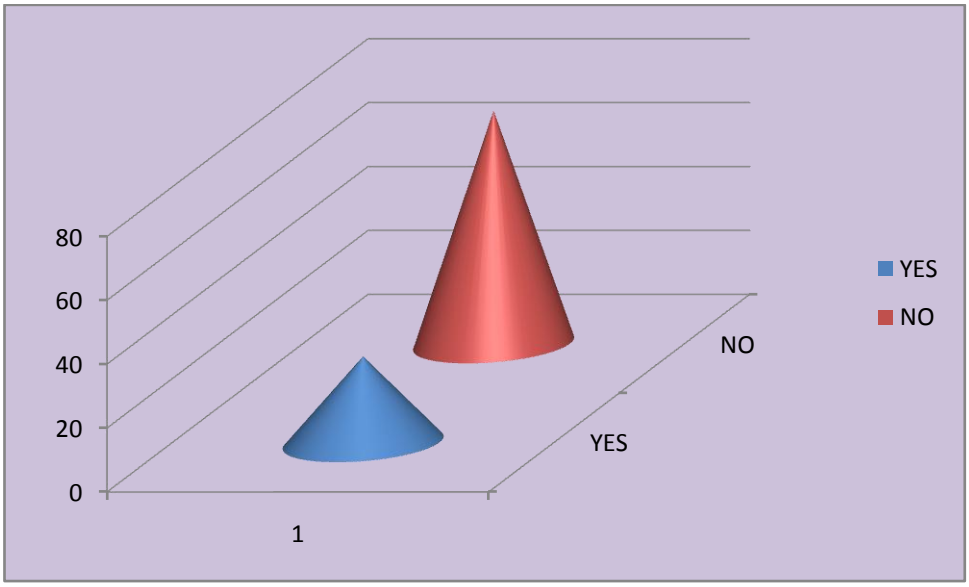


TABLE.18.

DISTRIBUTION OF BILIRUBIN

Bilirubin	Frequency	Percent
Abnormal	2	2.0
Normal	98	98.0
Total	100	100.0

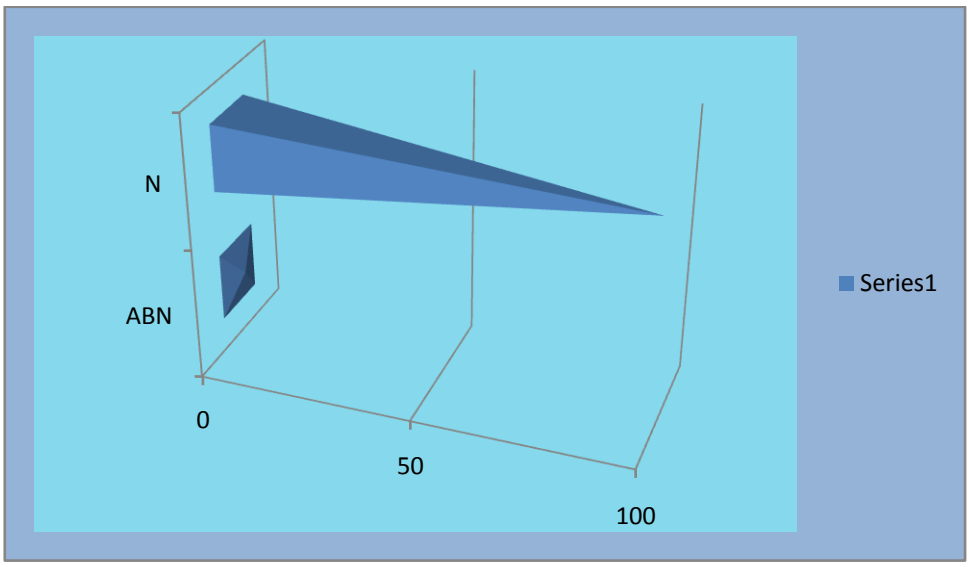


TABLE.19.

DISTRIBUTION OF SGOT AND SGPT

SGOT/ SGPT	Frequency	Percent
Abnormal	2	2.0
Normal	98	98.0
Total	100	100.0

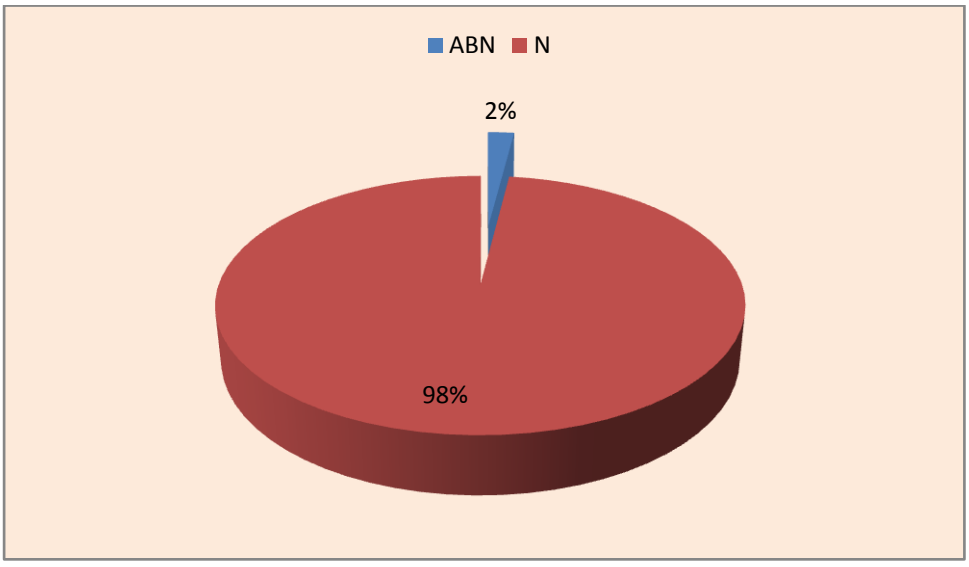


TABLE.20.

DISTRIBUTION OF SPUTUM A SAMPLE

Sputum A	Frequency	Percent
0	8	7.0
1+	43	43.0
2+	21	21.0
3+	18	18.0
SO2	5	5.0
SO4	1	1.0
SO5	3	3.0
SO6	1	1.0
Total	100	99.0
Total	100	100.0

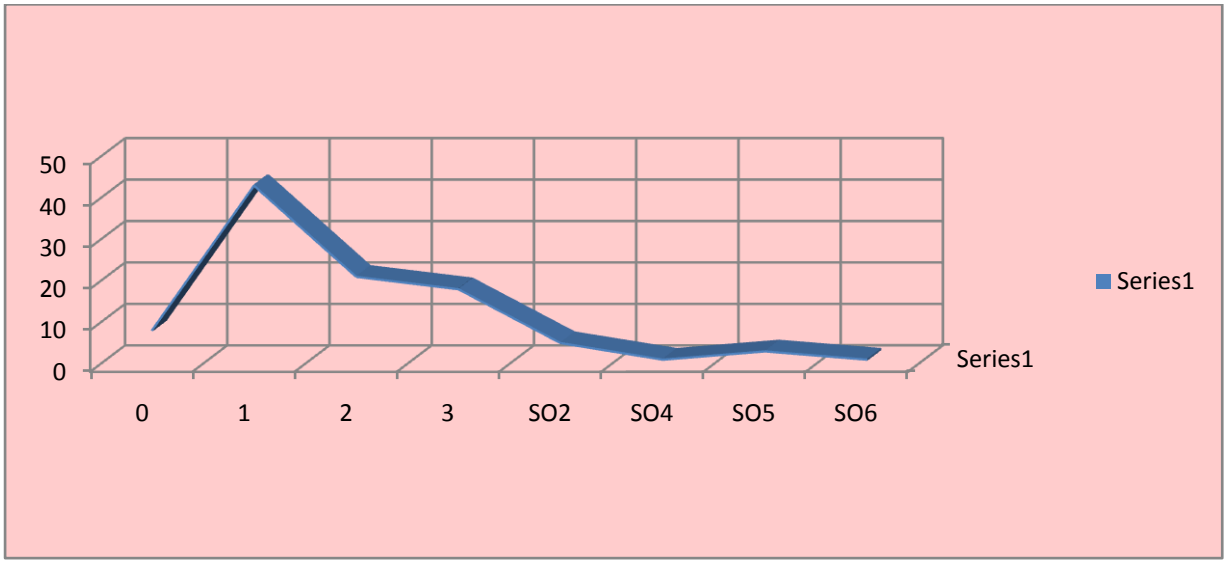
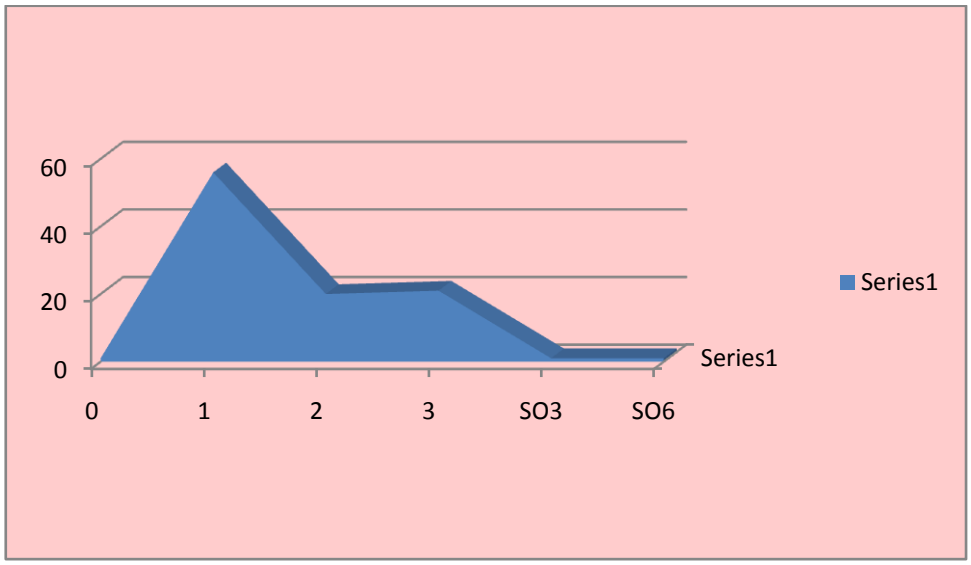


TABLE.21.

DISTRIBUTION OF SPUTUM B SAMPLE

Sputum B	Frequency	Percent
0	1	1.0
1+	56	56.0
2+	20	20.0
3+	21	21.0
SO3	1	1.0
SO6	1	1.0
Total	100	100.0



1. 73% of patients were anaemic.
2. Only 2% of patients were having abnormal Liver function test in view of raised S.Bilirubin, SGOT and SGPT levels.
3. In sample A, sputum for AFB 43% patients were having 1+, followed by 21%,18% for 2+ and 3+ viz.
4. In sample B, sputum for AFB 56% patients were having 1+, followed by 20%,21% for 2+ and 3+ viz.
5. All 100 patients are positive for AFB stain.

TABLE.22.

DISTRIBUTION OF UPPER ZONE INFILTRATION IN CHEST XRAY

Upper Zone Involvement	Frequency	Percent
NO	27	24.5
YES	73	66.4
Total	110	100.0

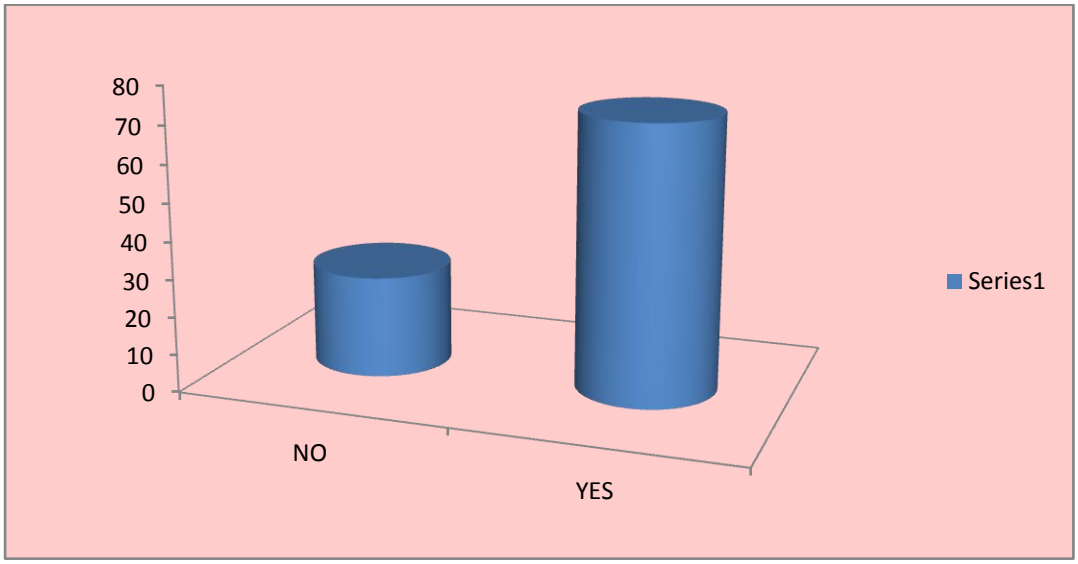


TABLE.23.

DISTRIBUTION OF MID ZONE INFILTRATION IN CHEST XRAY

Mid Zone	Frequency	Percent
NO	44	40.0
YES	56	50.9
Total	110	100.0

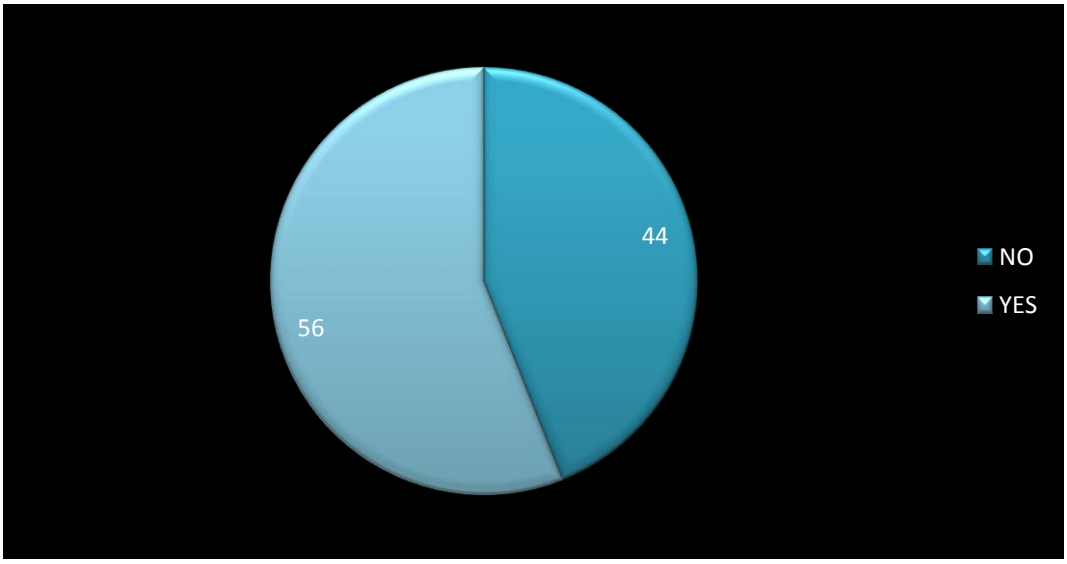


TABLE.24.

DISTRIBUTION OF LOWER ZONE INFILTRATION IN CHEST XRAY

Lower Zone	Frequency	Percent
NO	90	81.8
YES	10	9.1
Total	110	100.0

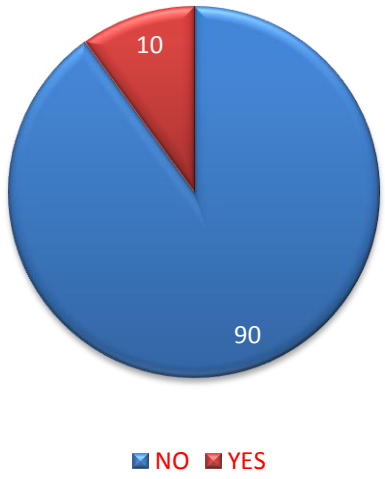
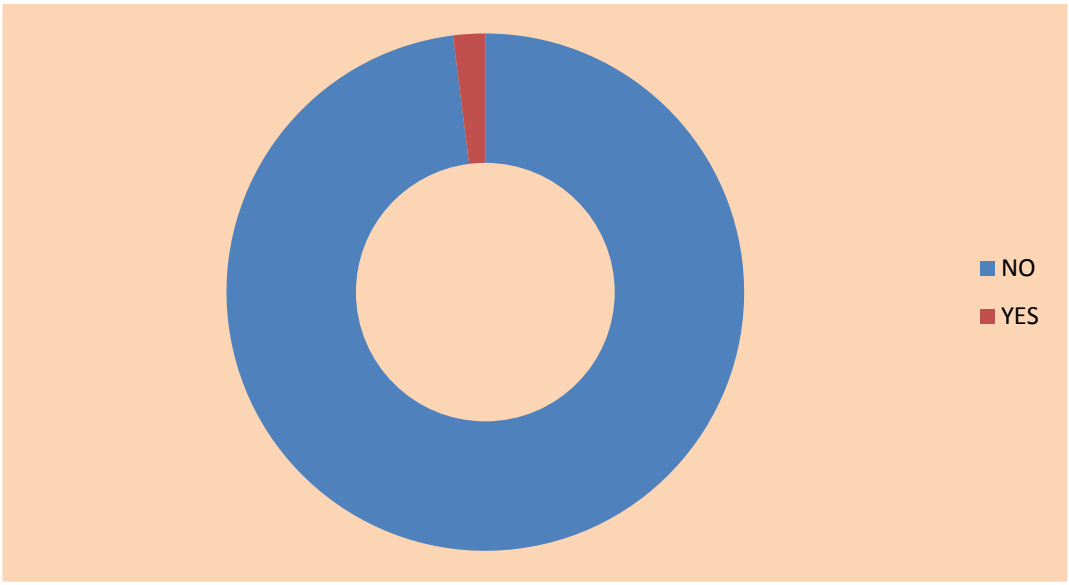


TABLE.25.

DISTRIBUTION OF RIFAMPICIN RESISTANCE

RIF Resistance	Frequency	Percent
NO	98	97.0
YES	2	3.0
Total	100	100.0



1. A total number of 73 patients, 66.4% were having Upper zone infiltration in Chest Xray.
2. With total number of 56 patients 50.9 were having Mid zone infiltration with upper zone in Chest Xray.
3. In10 patients,9.1% were having lower zone infiltration in Chest Xray.
4. Most commonly presented with upper zone consolidation or fibro cavity
5. Only 2% of patients are having Rifampicin Resistance have been identified by GeneXpert done for all 100 patients.

DISCUSSION

This study was conducted in Coimbatore medical college hospital from July 2014 to July 2015.This is a cross sectional type of study. In this study total number of 122 patients were taken and 100 patients were studied. 22 patients were excluded based on the exclusion criteria. The clinical and diagnostic findings of this study are compared with our studies in literature here.

Out of 100 patients, 84 patients were male and remaining 16 were female. Majority of patients were in the age group of 41-50 (25%) followed by 31-40(23%). And about 69% of patients were labourers and followed by drivers. There were 35% of smokers.

Most common symptom was cough (100%), followed by Cough with expectoration(93%),haemoptysis (64%) and fever (39%)..

Most common finding in general examination were pallor (67%) followed by poor nutrition(14%). And jaundice was seen in less than 2% patients.

In auscultatory findings were seen Crepitations (69%), Bronchial breath sounds (34%) and wheeze(27%) in viz.

And in laboratory findings anaemia seen in nearly 27% of patients, Elevated bilirubin , SGOT and SGPT levels are seen only 2%.

In Chest xray findings most commonly infiltrations seen in upper zone followed by middle and lower zones.

TABLE.26

COMPARISON OF SYMPTOMS BETWEEN THIS STUDY AND STUDY BY BIKARAM SINGH DATTA ET AL.

Symptoms	Present Study (%)	Bikaram Singh Datta et al[40] (%)
Cough	100	90.01
Haemoptysis	64	53
Fever	39	57.7
Constitutional Symptoms	70	61

The comparison of the above shows almost equal in symptoms except for fever which is high in bikaram Singh study. Likewise 100% cough seen in our present study.

Since the drug resistance in tuberculosis are increasing in trend globally, early detection of MDR-TB is essential.

In this study, only 2 patients were having Rifampicin resistance seen in out of 100 patients detected by using the GeneXpert.

Drug Resistance surveillance(DRS) were conducted at many of the states in our country such as Maharastra, Gujarat and Andhra Pradhesh and its results gives as the prevalence of MDR TB was about 2-3% in new cases and nearly 17% in old cases.

The drug resistance TB – surveillance and resistance report 2014 of WHO shows about 3.5% cases were MDR-TB in the globe.

Another study Sharma Et Al Prevalence Of Mdr-Tb in New Pulmonary Tuberculosis Cases estimated about 1.1 % for Rifampicin resistance.

And Lukoye D et al did the study on drug resistance new and previously treated sputum smear-positive tuberculosis patients in Uganda shows the Rifampicin resistance about 1.9%.

TABLE.27.

COMPARISON OF VARIOUS STUDIES INCLUDING WHO REPORT AND PRESENT STUDY

Authors	Total cases	Percent
Sharma Et al[37]	**177**	**1.1**
Lukoye D Et al[38]	**1209**	**1.9**
Kateruttanakul Et al[39]	**769**	**2.5**
Present Study	**100**	**2.0**

SUMMARY

- 122 cases of new smear positive TB patients are taken up for this study attending Out patient department at Coimbatore Medical College, Coimbatore. Out of which 100 cases are included for this study remaining are excluded as per criteria.
- Commonest age group involved in this study was 41-50 followed by 31-40.
- Males are most commonly affected(84%)
- Most commonly Laburers are commonly affected about 69%
- Cough(100%) followed by Expectoration, Haemoptysis and fever are the most common symptoms.
- Most common finding in respiratory examination was crepitations about 69%. And this alone present about 40% of patients. Wheezes were seen in 27% and bronchial breath sounds were seen in 34% of patients.
- Renal function test are normal for almost all patients.
- Totally 2 % of patients are having elevated S.Bilirubin, SGOT and SGPT
- Nearly 27% of patients are anemic.
- Most common finding in Chest X ray was infiltrations about 93%, total percent of cavitation was 38% and total percent of pleural effusion was 9%. And infiltration are most commonly seen in upper zone about 73% followed by mid zone involved about 56% and lower zone was 10%.
- Only 2% of patients sputum sample wee showing resistance to Rifampicin out of 100 patients.

CONCLUSION

1. In this study most common manifestations of New sputum pulmonary tuberculosis were cough with expectoration followed by fever, weight loss, haemoptysis. Most commonly upper zone of the lungs were involved. Most of the patients showed decreased haemoglobin, white blood cells and increases ESR.
2. Possibility of drug resistance is seen new smear positive pulmonary tuberculosis.
3. Resistance to Rifampicin were found in new sputum positive TB patients by using GeneXpert.
4. Prevalence of Drug resistance to Rifampicin in our locality is about 2%. to compare with national and international prevalence it was low.
5. Multi Drug Resistance Tuberculosis (MDR-TB) is described as the resistance to anyone of the first-line TB drugs Rifampicin and Isoniazid.
6. RIF resistance is the main indictor of MDR TB because the resistance to RIF mostly combined with the resistance for Isoniazid.
7. Since, this is the indicator for prevalence of MDR-TB and all new smear positive patients should be screened for the same to early detection, prevention of spread and management of MDR-TB.

Bibilography

1.Sakula A. Robert Koch (1843--1910): founder of the science of bacteriology and discoverer of the tubercle bacillus. A study of his life and work. *Br J Dis Chest.* 1979 Oct;73(4):389–394.

2.Gutierrez MC, Brisse S, Brosch R, Fabre M, Omais B, Marmiesse M et al. Ancient origin and gene mosaicism of the progenitor of Mycobacterium tuberculosis. PLoS Pathog 2005 Sep;1(1):e5.

3. Hershkovitz I, Donoghue HD, Minnikin DE, Besra GS, Lee OY, Gernaey AM et al. Detection and molecular characterization of 9000-year-old Mycobacterium tuberculosis from a neolithic settlement in the eastern mediterranean. PLoS ONE 2008;3(10):e3426.

4. Tuberculosis. Academic dictionaries and encyclopedias. [Online] 2006 [cited 2010 Sep 10]; Available from: URL:http://web.archive.org/web/20050211173218/http://classics.mit.edu/Hippocrates/aphorisms.mb.txt Aphorisms.

5. Al-Sharrah YA. The Arab Tradition of Medical Education and its Relationship withthe European Tradition. Springer 2003;33(4):413-25.

6. Bonah C. The experimental stable of the BCG vaccine: safety, efficacy, proof, and standards, 1921–1933. Stud Hist Philos Biol Biomed Sci 2005;36(4):696-721.

7. Nobel Foundation. The Nobel Prize in Physiology or Medicine 1905. [cited 2010 Sep10];

Availablefrom:URL:http://de.wikipedia.org/.../Simple:Nobel_Prize_in_Physiology_or_Medicine .

8. Kritski A, Cataldi A, Reyes A, Martin A, Gicquel B, Martin C et al. Tuberculosis

1. 2007. [cited 201

9. World Health Organization (2009). "Epidemiology" *Global tuberculosis control: epidemiology, strategy, financing*. pp. 6–33. ISBN 978-92-4-156380-2. Retrieved on12 November 2009.

10.http://www.who.int/tb/advisory_bodies/impact_measurement_taskforce/meetings/global_consultation_doc08a_who_methods_children.pdf

11. WHO annual report 2014 and 2015

12. http://www.tbcindia.nic.in/pdfs/TB%20INDIA%202014.pdf

13. http://www.who.int/tb/publications/global_report/gtbr14_supplement_web_v3.pdf

14. Emergence of Mycobacterium tuberculosis with extensive resistance to second-line
drugs, worldwide, 2000–2004. [Online] 2006 [cited 2010 July 12]; Available from: URL:http://www.ncbi.nlm.nih.gov/pubmed/16557213

15. Farmer P. The major infectious diseases in the world--to treat not to treat Engl. J. Med July 2001;345(3):208-10.

16. http://www.tbcindia.nic.in/rntcp.html

17. http://www.who.int/tb/strategy/en/

18. http://www.tbfacts.org/tb-india/

19.http://www.tbcindia.nic.in/pdfs/Guidelines%20for%20PMDT%20in%20India%20-%20May%202012.pdf

20.Harrison principle of Internal Medicine 19th edition

21.Color atlas of pathology pathological principle Dequela, Ursus-Nikolaus Riede,MD, Nartin Werner MD.,

22. American Thoracic society and centers for Disease control and Prevention.Diagnostic standards and classification of TB in adult and children.AM JRespir MED.2000:161

23. Robbins text book of Pathology

24. Crofton And Douglas's Respiratory Diseases by A. Gordon Leitch , Anthony Seaton , Douglas Seaton

25.Text book for Tuberculosis by surendra k Sharma

26.Drug-resistant tuberculosis. Iseman MD, Madsen LA [1989, 10(3):341-353]

27. Kekkaku. 1998 Nov;73(11):657-63.Multidrug-resistant tuberculosis. ,Ohno H[1], Koga H, Kohno S.

28. 2011www.who.int/tb/features_archive/xpert_rapid_tb_test/

29. Vijay S, Kumar P, Chauhan LS, Vollepore BH, Kizhakkethil UP,and Rao SG. Risk
factors associated with default among new smear positive TB patients treated under DOTS in India. PLoS ONE.April .2010;4(5): e10043.

30.ICMR Prevalence of drug resistance in patients with PT presenting for first time with symptoms at chest clinics in India ICMR 1969 57 823:35

31. Extensively drug resistant tuberculosis (XDR-TB): recommendations for prevention and control. Weekly Epidemiological Record 2008; 81(45):430-32.

32. API text book of Medcicne 10 th edition

33.http://www.lungindia.com/article.asp?issn=0970-2113;year=2013;volume=30;issue=4;spage=269;epage=272;aulast=Behera;aid=LungIndia_2013_30_4_269_120592s

34.SubhakarKandi, SurapaneniVenkateswara Prasad ,Prevalence of multidrug resistance among retreatment pulmonary tuberculosis cases in a tertiary care hospital,Hyderabad, IndiaYear : 2013 | Volume : 30 | Issue : 4 | Page : 277-279

35.Haji Khan Khoharo,1Imran Ali Shaikh2
Drug resistance patterns in pulmonary tuberculosis(JPMA 61:229; 2011).Vol. 61, No. 3, March 2011

36. Surendra K. Sharma, SanjeevKuma:Prevalence of multidrug-resistant tuberculosis among newly diagnosed cases of sputum-positive pulmonary tuberculosis:Indian J Med Res 133, March 2011, pp 308-31

37.Surendra K. Sharma, Sanjeev Kumar:
Prevalence of multidrug-resistant tuberculosis among Category II pulmonary tuberculosis patients
Indian J Med Res 133, March 2011, pp 312-315

38.Masoudshamei,Majidmarjani, First-line anti-tuberculosis drug resistance patterns and trends at the national TB referral center inIran——eight years of surveillanceInternational Journal of Infectious DiseasesVolume 13, Issue 5 , Pages e236-e240, September 2009

39. Anti-Tuberculosiss Drug Resistance among New and Previously Treated Sputum Smear-Positive Tuberculosis Patients in Uganda: Results of the First National Survey Deus Lukoye,
Published: August 1, 2013 DOI: 10.1371/journal.pone.0070763

40.Bikaram Datta *et al*. - Drug Resistant Tuberculosis in Kashmir, India *J Infect Dev Ctries* 2010; 4(1):019-023.

41. Review Article Indian J Med Res 120, October 2004, pp 377-386
C.N. Paramasivan & P. Venkataraman Tuberculosis Research Centre (ICMR),Chennai, India.

ANNEXURE

A.1 PROFORMA

Name		Age	
Occupation		Sex	
Socio Economic status		TB No./IP No.	
Address			
		Yes	no
Clinical symptoms	Cough		
	Expectoration		
	Haemoptysis		
	Fever		
	others		
	Contact with TB		
Past History	DM/SHT/CAD etc.		
Clinical Examination	Pallor		
	Jaundice		
	Nutrition		
	Pedal Edema		
	Fever		
Respiratory System findings	Crepitations		
	Wheeze		
	Bronchial breath sounds		
Blood Investigations	Haemoglobin		
	ESR		
	Total Count		
	Differential Count		
	Random Blood Sugar		
	B.Urea		
	S.Creatinine		
	Liver Function Tests	Bilirubin T & D	
		SGOT	
		SGPT	
		T.Proteins	
		Albumin	
		Globulin	
	HIV I & II		
Sputum for AFB			
Chest Xray PA view			
GENE XPERT CBNAAT for RIF			

A.2 CONSENT FORM

Yourself Mr./Mrs./Ms…….. are being asked to be a participant in the research study titled "A Study of Drug Resistance TB among patients with New Sputum Smear Positive Pulmonary Tuberculosis patients"in CMC Hospital, Coimbatore, conducted by DR.BHARATHIRAJA.G., Post Graduate Student, Department of General Medicine, Coimbatore Medical College. You are eligible after looking into the inclusion criteria. You can ask any question you may have before agreeing to participate.

Purpose of Research

1.To determine the prevalence of Drug resistance (Rifampicin)in New smear sputum positive patients during study period.

2.To determine the drug resistance pattern among them by using Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) [GeneXpert] .

3.To analyze the drug resistance of New smear sputum positive Patients to decide whether the DOTS PLUS regimen should start early.

Research Being Done

"A Study of Drug Resistance TB among patients with New Sputum Smear Positive Pulmonary Tuberculosis patients"

Decline from Participation

You have the option to decline from participation in the study existing protocol for your condition.

Privacy and Confidentiality

Privacy of individuals will be respected and any information about you or provided by you during the study will be kept strictly confidential.

Authorization to publish Results

Results of the study may be published for scientific purposes and/or presented to scientific groups, however you will not be identified.

Statement of Consent

I volunteer and consent to participate in this study. I have read the consent or it has been read to me. The study has been fully explained to me, and I may ask questions at any time.

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Signature /Left thumb impression (volunteer)	Date
----------	----------
Signature of witness	Date

Sl no	LAB NO/TB	AGE	SEX	OCCUP	CLINICAL SYMPTOMS					ICAL EXAMINAT		BLOOD ROUTINE			LFT		RFT	C-X RAY			SPUTUM AFB	HIV 1 & 2	CB NAAT (GENE XPERT)	
					COUGH	EXPECTO	HAEMO	FEVER	OTHERS	GI	RSE	Hb(gm%	TC/DC	ESR	BILI	SGOT	BU/SrCr	UZ	MZ	LZ	SEPECIMEN A/B		POSTIVE FOR	RESISTANCE TO RIF
1	535/169	60	M	LAB	YES	YES	NO	NO	WL		Crps	11	9600/P62,L36	44	N	N/N	24/0.9	IN,C			1+/2+	NEG	YES	
2	651/369	47	M	DRI	YES	YES	YES	YES			Wh/Crpts	12	5400/P44,L54	32	N	N/N	32/0.6		IN,C		S05/1+	NEG	YES	
3	716/111	60	M	LAB	YES	YES	YES	YES	WL	P	Crpts	8.9	4500/P50,L40	45	N	N/N	28/1.0	IN			2+/3+	NEG	YES	
4	907/21	17	F	STU	YES	YES	NO	YES	WL	P	Wh	9.2	5600/P67/L32	47	N	N/N	26/0.8		IN		1+/1+	NEG	YES	
5	525/327	39	M	LAB	YES	YES	NO	NO		P	Crpts	8.4	8800/P58,L37	44	N	N/N	29/1.2	IN,C	IN		3+/3+	NEG	YES	
6	717/315	31	M	DRI	YES	YES	YES	NO		P,PN	Wh/BB	9.8	7400/P60,L36	26	N	N/N	34/0.9	IN	C		1+/S03	NEG	YES	
7	520/311	20	F	STU	YES	YES	NO	YES	WL	P	Crpts	8.6	8200/P50/L47	38	N	N/N	26/0.5		IIN		1+/1+	NEG	YES	
8	455/101	48	M	LAB	YES	YES	NO	YES	WL	P	Wh/BB	10.2	7200/P42,L56	42	N	N/N	32/0.8	IN			1+/1+	NEG	YES	
9	454/409	36	M	LAB	YES	YES	NO	NO			Crpts	12.6	6700/P54,L44	33	N	N/N	28/0.9	IN			3+/2+	NEG	YES	
10	350/210	27	M	DRI	YES	YES	YES	NO	WL	P,PN	Wh/BB	9.8	5600/P67/L32	31	N	N/N	32/0.6		IN		2+/2+	NEG	YES	
11	453/226	35	M	LAB	YES	YES	NO	YES			Crpts	13	4200/P62,L36	42	N	N/N	26/0.7	IN	C		1+/1+	NEG	YES	
12	452/233	29	M	LAB	YES	YES	NO	NO	WL		Wh	10.9	5800/P56,L42	35	N	N/N	33/0.9		IN		2+/3+	NEG	YES	
13	338/641	55	F	HM	YES	YES	YES	NO	WL	P	Crpts/BB	9.2	6600/P42,L56	24	N	N/N	27/0.7	IN			1+/1+	NEG	YES	RESISTANCE TO RIF
14	2.32E+09	27	M	LAB	YES	YES	YES	NO	WL	P	Crepts	10.1	6800/P70/L28	36	N	N/N	25/0.9	IN			1+/1+	NEG	YES	
15	113/382	60	M	LAB	YES	YES	NO	YES			Wh	13	4600/P72/L27	25	N	N/N	36/0.6	IN			S02/1+	NEG	YES	
16	110/261	28	M	DRI	YES	YES	NO	NO	WL	P	Crpts/Wh	10.5	5600/P67/L32	26	N	N/N	27/0.8	IN			1+/1+	NEG	YES	
17	111/388	45	M	LAB	YES	YES	YES	NO	WL	P	Crpts/BB	10.7	10700/P42/L5	47	N	N/N	36/0.9	IN,C	IN		2+/3+	NEG	YES	
18	1215/144	23	M	LAB	YES	YES	NO	NO	WL	P	Wh	9.7	4700/P57,L37	18	N	N/N	30/1.1		IN		1+/1+	NEG	YES	
19	455/96	36	M	LAB	YES	YES	NO	NO	WL		Crpts	10.2	5700/P70/L29	26	N	N/N	27/0.9	IN			1+/SO6	NEG	YES	
20	114/194	18	F	STU	YES	YES	NO	NO	WL	P	Crpts/Wh	9.2	6300/P60/L37	31	N	N/N	26/0.6	IN	IN		1+/2+	NEG	YES	
21	456/107	42	M	DRI	YES	YES	YES	YES		P	Wh/BB	8.8	8900/P50/L47	36	N	N/N	32/0.8	IN	C		2+/1+	NEG	YES	
22	906/360	65	M	LAB	YES	YES	NO	NO	WL	P	Crpts/BB	10.3	9700/P40/L57	45	N	N/N	40/1.2	,C	IN		S06/1+	NEG	YES	RESISTANCE TO RIF
23	350/165	64	M	LAB	YES	YES	YES	NO	WL	P,PN	Crpts/BB	9.1	11050/P36,L62	60	N	N/N	42/2	IN	C		2+/2+	NEG	YES	
24	697/427	38	M	LAB	YES	YES	NO	YES	WL		Crpts	12	7500/P57,L32	36	N	N/N	36/0.7	IN			1+/1+	NEG	YES	
25	116/180	65	M	LAB	YES	YES	YES	YES	WL	P,PN	Crpts	10	4500/P50,L40	40	N	N/N	23/0.9	IN			3+/2+	NEG	YES	
26	117/296	42	F	HM	YES	YES	NO	YES		P	Crpts/Wh	9	6100/P60,L36	35	N	N/N	25/0.8		IN		3+/1+	NEG	YES	
27	353/269	52	M	LAB	YES	YES	YES	YES	BLS	P	Crpts/BB	8	6500/P50,L40	55	N	N/N	36/1	IN,C			NEG/1+	NEG	YES	
28	706/35	37	M	LAB	YES	YES	YES	YES	WL	P,PN	Crpts/BB	8	10720/P50,L47	57	N	N/N	40/2	IN,C	IN	PLE	2+/2+	NEG	YES	
29	1003/100	52	M	DRI	YES	YES	NO	NO			Crpts	11	5500/P60,L37	43	N	N/N	32/0.6		IN		3+/3+	NEG	YES	
30	1411/326	43	M	LAB	YES	NO	NO	NO		P		12	6450/P50,L40	28	N	N/N	23/0.1		IN		NEG/1+	NEG	YES	
31	694/219	40	M	LAB	YES	YES	NO	NO		P	Crpts	9	6000/P55,L30	15	N	N/N	36/0.7				2+/1+	NEG	YES	

32	120/47	34	F	HM	YES	YES	YES	NO	WL	P,PN	Crpts/BB	8	9070/P40,L60	58	1.8	40/4	40/1.4	IN,C	IN	IN	1+/2+	NEG	YES	
33	1382/94	48	F	LAB	YES	NO	NO	YES	WL	P	Wh	10	6700/P40,L57	20	N	N/N	34/0.6	IN			3+/3+	NEG	YES	
34	1432/145	34	M	DRI	YES	YES	NO	NO	WL	P,PN	Crpts	8	7500/P35L65	60	N	N/N	43/1	IN	C		2+/1+	NEG	YES	
35	1373/388	42	F	HM	YES	YES	NO	NO			Crpts	11	8600/P55,L30	30	N	N/N	40/1		IN		2+/3+	NEG	YES	
36	600/54	45	M	LAB	YES	YES	YES	YES	WL	P	Wh/BB	9.6	6800/P66.L34	36	N	N/N	38/1.2		IN,C		S05/1+	NEG	YES	
37	1369/364	38	F	LAB	YES	NO	YES	YES	WL	P,PN	Crpts/BB	8	10100/P40,60	65	N	N/N	42/2	IN,C	IN		1+/2+	NEG	YES	
38	1485/4033	39	M	LAB	YES	YES	YES	NO		P	Crpts/BB	9	12000/P45,L55	56	2.6	56/7	36/.9	IN,C	C		NEG/1+	NEG	YES	
39	1377/106	45	M	LAB	YES	YES	NO	NO			Wh	12	5700/P50,L45	36	N	N/N	24/1.1		IN		1+/2+	NEG	YES	
40	1371/259	22	M	DRI	YES	YES	NO	NO	WL	P	BB/Wh	9.5	1220/P60,L35	30	N	N/N	37/1.2	IN	C	IN	S02/1+	NEG	YES	
41	1012/389	31	M	LAB	YES	YES	YES	YES	BLS	P	Crpts/BB	10.5	1350/P50,L47	60	N	N/N	26/1.0	IN,C	IN		1+/1+	NEG	YES	
42	1379/53	40	M	LAB	YES	YES	YES	NO	WL	P	Wh/BB	10.5	6070/P50,L46	28	N	N/N	36/0.6	IN			3+/2+	NEG	YES	
43	6150/116	57	M	LAB	YES	YES	NO	YES		P	Crpts/BB	10	5700/P58,L40	55	N	N/N	35/1.6	IN,C		IN	3+/3+	NEG	YES	
44	123/87	60	M	LAB	YES	YES	NO	NO			Crpts	13	6050/P70/L30	30	N	N/N	30/0.8	IN,	IN		1+/2+	NEG	YES	
45	115A	23	M	LAB	YES	YES	NO	NO	WL		Crpts	13	7000/P60/L37	26	N	N/N	36/0.7	IN			1+/1+	NEG	YES	
46	170A	32	M	DRI	YES	YES	YES	YES	WL	P	Crpts/BB	9	12000/P40/L5	62	N	N/N	40/1.2	IN,C	IN		1+/1+	NEG	YES	
47	153A	55	M	LAB	YES	YES	NO	YES		P	Crpts	9.2	8200/P50/L47	41	N	N/N	36/0.9	IN			1+/1+	NEG	YES	
48	163B	47	M	LAB	YES	YES	NO	NO	WL		Crpts	12	5700/P60/L35	26	N	N/N	26/0.8		IN		3+/3+	NEG	YES	
49	152B	27	M	LAB	YES	NO	NO	NO	WL		Crpts	13.2	4200/P57/L32	36	N	N/N	27/0.9	IN			2+/3+	NEG	YES	
50	111B	60	M	LAB	YES	YES	YES	NO	WL	P	Crpts	9	6800/P42/L52	30	N	N/N	27/0.8	IN			S02/1+	NEG	YES	
51	454/303	47	M	DRI	YES	YES	NO	YES	WL	P	Wh/BB	9.8	5400/P45,L49	44	N	N/N	24/1.1	IN,C			1+/2+	NEG	YES	
52	112B	39	M	DRI	YES	YES	NO	NO			Crpts	13	4200/P45/L53	26	N	N/N	36/0.7				1+/2+	NEG	YES	
53	62A	70	M	LAB	YES	YES	NO	YES	WL	PN	Crpts/BB	12	4600/P60/L35	36	N	N/N	36/1.1	IN	C		3+/3+	NEG	YES	
54	61B	40	M	LAB	YES	YES	NO	NO		P		10.2	5200/P65/L30	38	N	N/N	26/0.7				2+/2+	NEG	YES	
55	63A	5	M	LAB	YES	YES	NO	NO	WL	P	Crpts	9.3	5300/P67/L30	45	N	N/N	36/0.6	IN			S04/1+	NEG	YES	
56	40A	53	M	DRI	YES	YES	NO	NO		P	Crpts/Wh	10.2	4200/P45/L53	41	N	N/N	31/1.2	IN			1+/1+	NEG	YES	
57	46B	54	M	LAB	YES	YES	YES	NO	WL	PN	Crpts	12	1150/P70,L30	36	N	N/N	27/1.1	IN	C		NEG/1+	NEG	YES	
58	45B	26	M	STU	YES	YES	NO	NO		P		10	4200/P70,L26	30	N	N/N	31/0.9	C			NEG/1+	NEG	YES	
59	43A	55	M	LAB	YES	YES	NO	NO	WL	P	Crpts/BB	9	10200/P36,l63	52	N	N/N	41/1.2	C			3+/2+	NEG	YES	
60	699/312	35	F	HM	YES	YES	YES	YES	WL	P,PN	Crpts,Wh	9.2	8400/P48,L44	41	N	N/N	33/0.7	IN			3+/3+	NEG	YES	
61	77A	50	M	LAB	YES	YES	NO	YES	WL	P	Crpts	9.2	12200/P45,L54	40	N	N/N	36/1.7	IN	IN		1+/1+	NEG	YES	
62	78B	48	M	LAB	YES	YES	NO	NO			Wh	14	6350/P72,L26	15	N	N/N	26/0.7		IN		1+/2+	NEG	YES	
63	79B	63	M	LAB	YES	YES	NO	YES		P	Wh	8.8	4700/P57,L37	22	N	N/N	27/0.8	IN			1+/3+	NEG	YES	
64	80A	35	M	DRI	YES	YES	NO	YES	WL		Crpts	12	5400/P60,L37	41	N	N/N	36/0.8	C	IN		3+/1+	NEG	YES	

65	93B	50	M	LAB	YES	YES	YES	NO	WL	P	Wh	10	4750/P65,L34	30	N	N/N	30/0.9			IN	1+/1+	NEG	YES	
66	42B	25	F	STU	YES	YES	NO	YES	WL	P	Crpts	9.4	9720/P55,L42	36	N	N/N	32/0.7	IN			S02/1+	NEG	YES	
67	41A	44	M	LAB	YES	YES	YES	NO			Crpts/BB	12.8	10200/P36,l63	20	N	N/N	31/0.6	C	IN,C		1+/1+	NEG	YES	
68	67A	38	M	LAB	YES	YES	NO	NO	WL		BB	12.8	6350/P53,L46	22	N	N/N	32/1.2	IN			1+/NEG	NEG	YES	
69	66A	31	M	LAB	YES	YES	NO	NO	WL	P	Wh	10	5500/P60,L40	36	N	N/N	21/0.6		IN		2+/1+	NEG	YES	
70	64A	48	M	LAB	YES	YES	YES	NO	WL	P	Crpts/BB	9	11200/P40,L57	42	N	N/N	36/1.1		IN,C	IN	1+/1+	NEG	YES	
71	76B	19	M	STU	YES	YES	YES	YES		P	Crpts	10	10100/P36,L63	46	N	N/N	38/1.0	IN			1+/3+	NEG	YES	
72	84	32	m	STU	YES	YES	NO	YES	WL	P	Crpts	8.6	8200/P50/L47	38	N	N/N	26/0.5		IIN		1+/1+	NEG	YES	
73	102	23	m	HM	YES	YES	NO	YES		P	Crpts/Wh	9	6100/P60,L36	35	N	N/N	29/0.9	C	IN		3+/1+	NEG	YES	
74	125	19	F	LAB	YES	NO	NO	YES	WL	P	Wh	10	8700/P40,L57	20	N	N/N	34/0.6	IN			NEG/1+	NEG	YES	
75	132	74	M	DRI	YES	YES	NO	NO	WL	P,PN	Crpts	8	9500/P35L65	60	N	N/N	41.5/1.1	IN	C		2+/1+	NEG	YES	
76	98	56	F	LAB	YES	YES	YES	NO	WL	P	Crpts/BB	9.7	10700/P42/L5	47	N	N/N	36/0.9	IN,C	IN		2+/2+	NEG	YES	
77	56	43	M	LAB	YES	YES	NO	NO	WL	P	Wh	11.7	6900/P58,L32	28	N	N/N	18/0.6		IN		1+/1+	NEG	YES	
78	61	29	M	STU	YES	YES	NO	NO			Crpts	11	11600/P55,L35	42	N	N/N	20/1.0	C	IN		NEG/1+	NEG	YES	
79	142	19	M	LAB	YES	YES	YES	YES	WL	P	Wh/BB	12.6	12800/P56.L44	56	N	N/N	39/1.3		IN,C		S05/1+	NEG	YES	
80	150	41	M	LAB	YES	NO	YES	YES	WL	P,PN	Crpts/BB	8	9100/P40,L 60	34	N	N/N	26/0.5	IN,C	IN		2+/1+	NEG	YES	
81	152	54	M	LAB	YES	YES	NO	YES		P	Crpts	10.2	8200/P50/L47	41	N	N/N	36/0.9	IN			1+/1+	NEG	YES	
82	158	32	M	LAB	YES	YES	NO	NO	WL		Crpts	12	5700/P60/L35	26	N	N/N	26/0.8		IN		3+/3+	NEG	YES	
83	171	48	F	LAB	YES	NO	NO	NO	WL		Crpts	14	7200/P57/L32	36	N	N/N	27/1.0	IN			2+/3+	NEG	YES	
84	186	61	M	LAB	YES	YES	YES	NO	WL	P	Crpts	9	6800/P42/L52	30	N	N/N	27/0.8	IN			S02/1+	NEG	YES	
85	190	33	M	DRI	YES	YES	NO	YES	WL	P	Wh/BB	9.8	5400/P45,L49	44	N	N/N	24/1.1	IN,C			1+/3+	NEG	YES	
86	191	47	M	LAB	YES	YES	NO	NO			Crpts	12.8	7700/P54,L44	33	N	N/N	28/0.9	C,IN			3+/1+	NEG	YES	
87	199	22	F	DRI	YES	YES	YES	NO	WL	P,PN	Wh/BB	9	6600/P67/L32	48	N	N/N	34/0.9		IN		2+/3+	NEG	YES	
88	204	39	M	LAB	YES	YES	NO	YES			Crpts	13	9400/P62,L36	64	N	N/N	32.5/0.8	IN	C		1+/1+	NEG	YES	
89	206	49	M	LAB	YES	YES	NO	NO	WL		Wh	10.9	5800/P56,L42	35	N	N/N	33/0.9	C	IN		2+/3+	NEG	YES	
90	211	27	M	LAB	YES	YES	NO	NO		P		9.2	5900/P65/L30	38	N	N/N	29/1.1	C		IN	2+/2+	NEG	YES	
91	216	21	M	LAB	YES	YES	NO	YES		P	Crpts/BB	10	7800/P58,L40	80	N	N/N	42/1.6	IN,C		IN	3+/3+	NEG	YES	
92	219	59	M	LAB	YES	YES	NO	NO			Crpts	13	10050/P70/L3	94	N	N/N	30/1.0	IN,C	IN		1+/2+	NEG	YES	
93	223	71	M	LAB	YES	YES	NO	NO	WL		Crpts	13	9800/P60/L37	46	N	N/N	29/0.7	IN			1+/1+	NEG	YES	
94	224	65	M	DRI	YES	YES	YES	YES	WL	P	Crpts/BB	8	13500/P40/L5	112	N	N/N	47/1.9	IN,C	IN		1+/1+	NEG	YES	
95	230	40	F	LAB	YES	YES	NO	YES		P	Crpts	8.2	8200/P50/L47	42	N	N/N	37/0.5	IN			1+/1+	NEG	YES	
96	236	19	M	LAB	YES	YES	NO	NO	WL		Crpts	14	10700/P60/L3	26	N	N/N	41/1.5	C	IN		3+/3+	NEG	YES	
97	237	28	M	LAB	YES	YES	YES	NO			Crpts/BB	12.8	10200/P36,l63	20	N	N/N	31/0.6		IN,C		1+/1+	NEG	YES	

98	240	36	M	LAB	YES	YES	NO	NO	WL		BB	12.8	7500/P53,L46	22	N	N/N	18/0.7	IN			NEG/1+	NEG	YES	
99	242	52	M	LAB	YES	YES	NO	NO	WL	P	Wh	10	7100/P60,L40	56	N	N/N	27/0.6		IN		2+/1+	NEG	YES	
100	245	49	M	LAB	YES	YES	YES	NO	WL	P	Crpts/BB	7.5	12200/P40,L57	108	N	N/N	34/1.3	C	IN,C	IN	1+/1+	NEG	YES	

KEY ABBREVIATIONS FOR THE MASTER CHART

BB - Bronchial breathing

BU/SrCr - Blood Urea/Serum Creatine

CXR-UZ - Chest X-ray upper zone

CXR-MZ - Chest X-ray middle zone

CXR-LZ - Chest X-ray lower zone

Crpts - Crepitations

C - Cavitation

DRI - Driver/Conductor

ESR - Erythrocyte sedimentation rate

FAR - Farmer

F - Female

GPE - General physical Examination

Hb(%) - Heamoglobin

HM - House maker

IN - Infiltration

Ict - Icterus

Lab/TB No - Laboratory/tubercular number

LAB - Labourer

M - Male

N - Normal

OT - SGOT

PT - SGPT

P - Pallor

PLE - Pleural effusion

PN - Poor nutrition

R - Resistance

RSE - Respiratory system Examination

SL No - Serial number

S - Sensitive

STU - Student

TC/DC - Total Count / Differential Count

Wh - Wheezes

WL - Weight Loss

S - Streptomycin

H - Isoniazid

R - Rifampicin

Z - Pyrazinamide

E - Ethambutol

Km - Kanamycin

Ofx - Ofloxacin

Eth - Ethionamide