

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

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### **Abstract :**

Multidrug-resistant tuberculosis (MDR-TB) has emerged as a significant global health concern. Especially in India, emergence of drug resistant tuberculosis (TB), particularly multidrug resistant TB (MDR-TB) and extensively drug resistant TB (XDR-TB) is a major concern. India is the country having second highest burden of MDR-TB cases following China. Although progress has been made to reduce global incidence of drug-susceptible tuberculosis, the emergence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis during the past decade threatens to undermine these advances. Reported that India has approximately 66,000 MDR-TB cases among notified pulmonary TB cases in 2011 (new cases - 21,000 with a range of 15,000-27,000 and retreatment cases - 45,000 with a range of 40,000-50,000). Various surveys done in India by well-qualified and accredited laboratories revealed that MDR-TB in new cases is about 2.1% (1.5-2.7) and is about 15% in retreatment cases. Globally, about 9% of all MDR cases are XDR-TB. Even though patients are previously treated for TB is the most important risk factor for development of MDR-TB. New sputum smear positive tuberculosis patients having the risk of either one of spontaneous mutations or transmission of drug-resistant strains for developing single or multi drug resistance. Unfortunately we did not have any studies about the prevalence of MDR-TB among new cases of sputum-positive pulmonary TB. Category II pulmonary TB are including those who treatment failure, relapse after treatment, or default. Newer diagnostic tests like Cartridge Based Nucleic Acid Amplification Test (CB-NAAT) [GeneXpert] and / or Line Probe Assay (LPA) are the novel integrated tests for the diagnosis of tuberculosis and rapid detection of RIF and INH resistance in pulmonary and extra pulmonary specimens obtained from possible tuberculosis patients.

If we find earlier whether they have drug resistance, we can start the treatment for MDR-TB as soon as possible. Starting treatment for drug resistance earlier, we can save the money for the nation and improve the mortality and morbidity of TB patients.

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### **I. Introduction**

Tuberculosis (TB) is an infectious disease which spread by Mycobacterium tuberculosis. TB primarily usually infects 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, it 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 possess good anti mycobacterial 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.

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

## **II. Materials And Methods**

### **2.1 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.

**2.2 design Of Study:** Cross Sectional Study.

**2.3 period Of Study:** One year, July 2014 - June 2015.

**2.4 sample Size:** 100

### **2.5 Inclusion Criteria:**

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

2. Age above 18 yrs.

### **2.6 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).

### **2.7 Methodology**

The study is will be undertaken on the patients attending medicine out patient 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 immunosuppressions. 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.

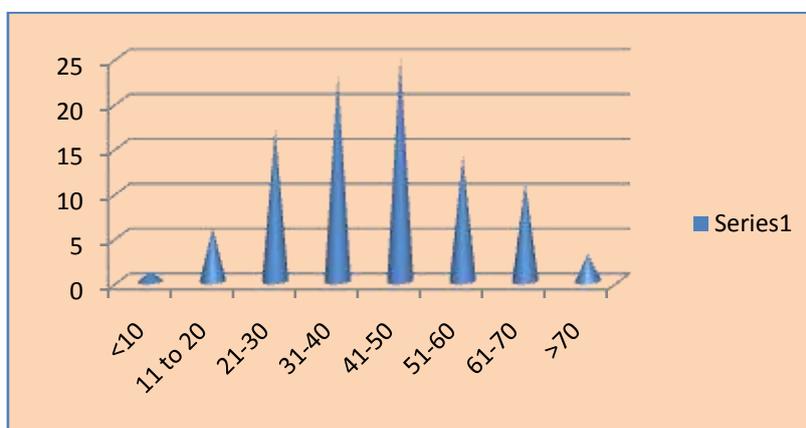
**2.8 Investigations:**

- 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)

**III. Figures And Tables**

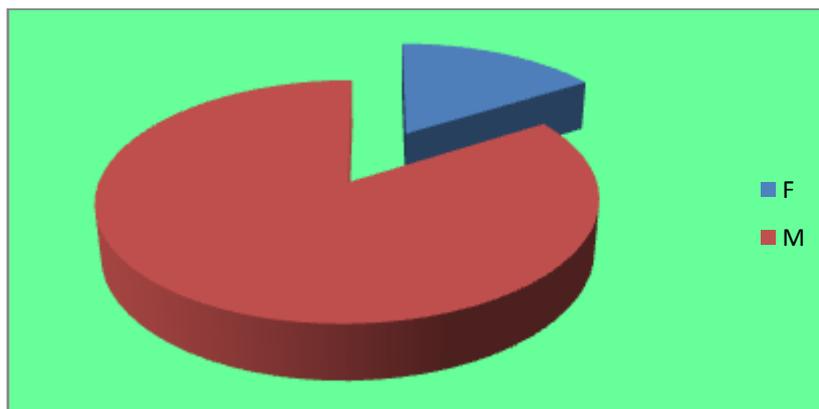
**Table 1.** DistributionOf Age

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



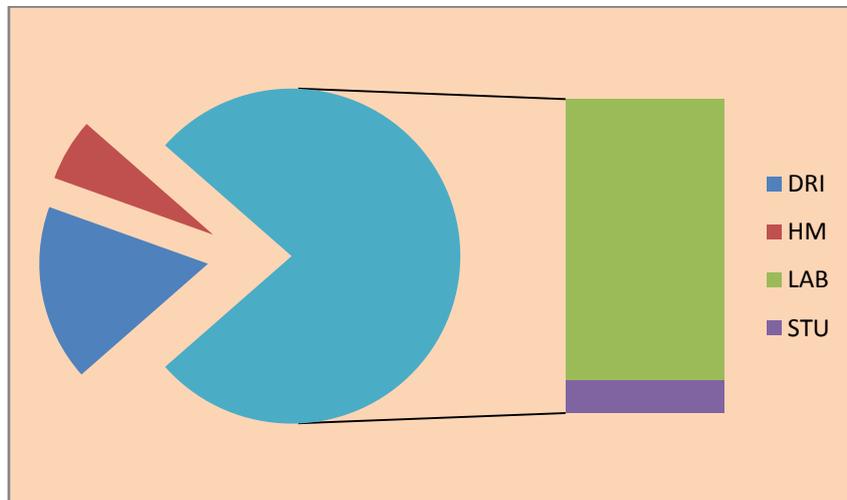
**Table 2** Distribution Of Sex

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



**Table 3** 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

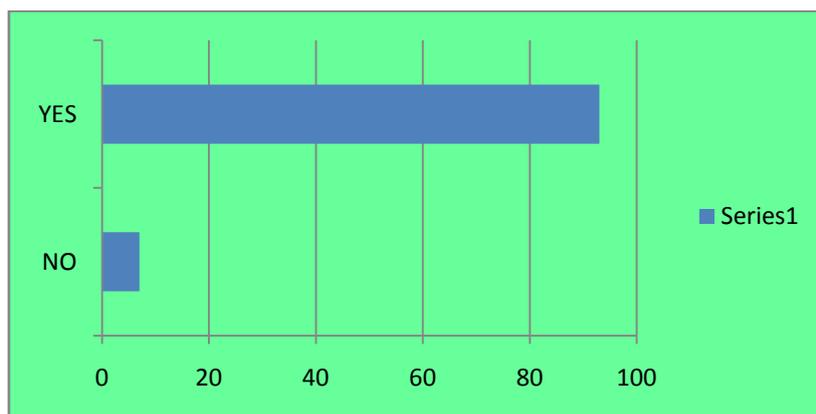
**Table.4.** Distribution of Cough

Cough	Frequency	Percentage
YES	100	100.0



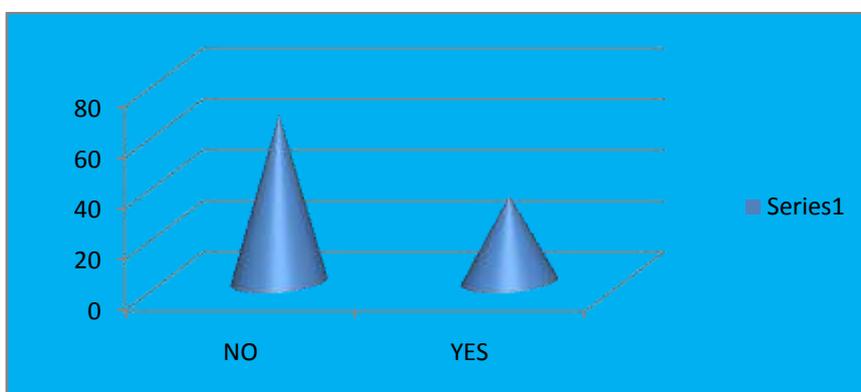
Cough with Expectoration	Frequency	Percent
NO	7	7.0
YES	93	93.0
Total	100	100.0

**Table .5.**Distribution of Cough Expectoration



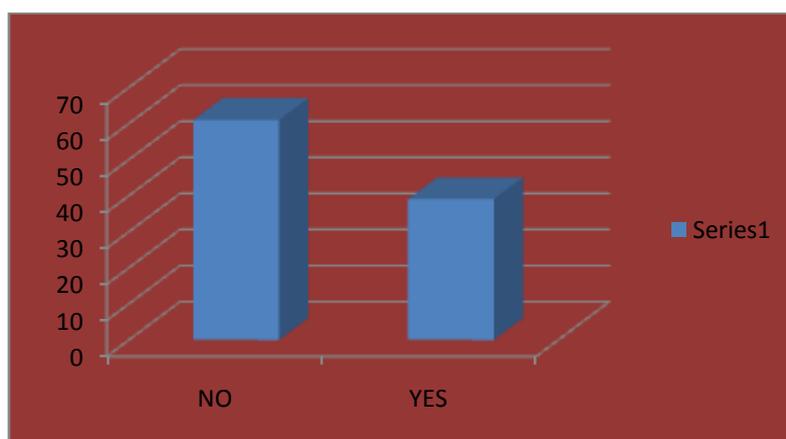
**Table.6.** Distribution of Haemoptysis

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



**Table.7.**Distribution of Fever

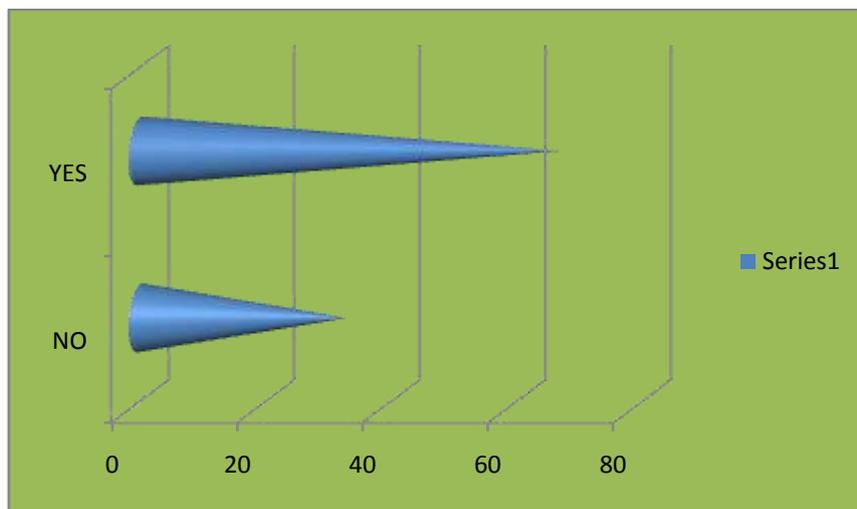
Fever	Frequency	Percentage
NO	61	61.0
YES	39	39.0
Total	100	100.0



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 Commonsymptom with which patients were presented with Cough (100%) followed by expectation (93%).

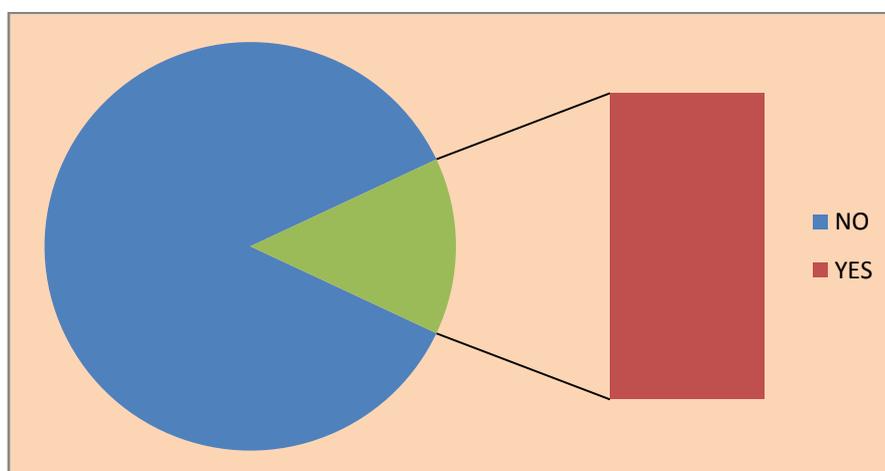
**Table No.8.** Distribution of Pallor in General Examination

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



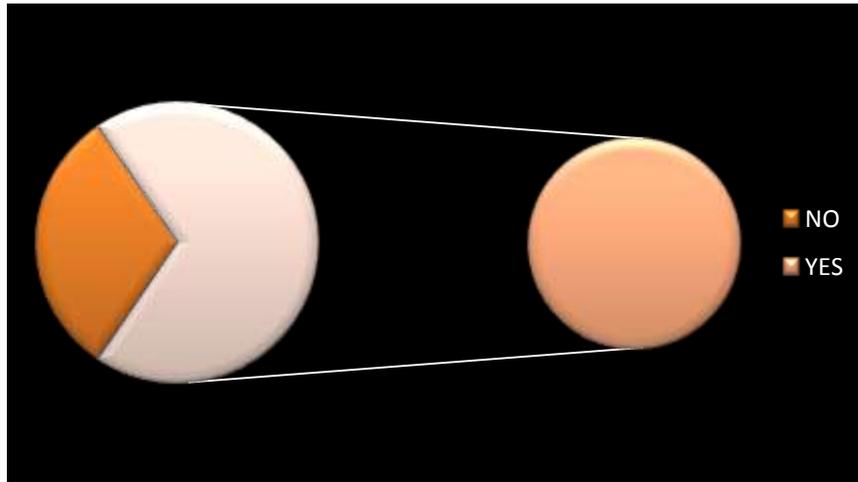
**Table.9.** Distribution of the Poor Nutrition

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



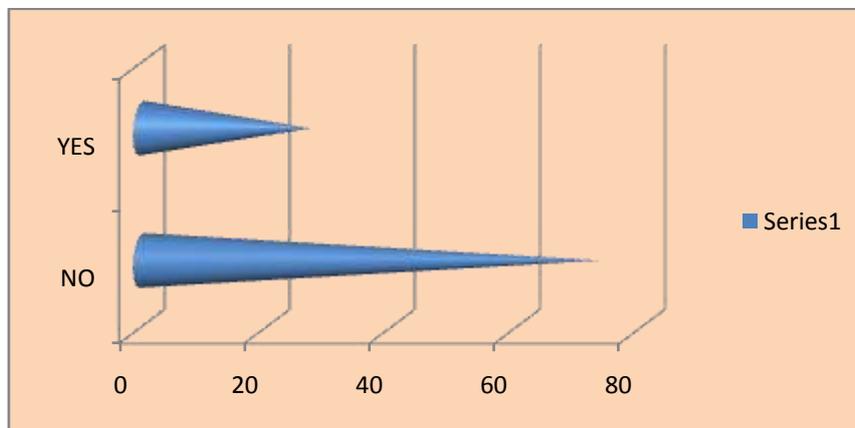
**Table.10.** Distribution of Crepitations (Respiratory finding)

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



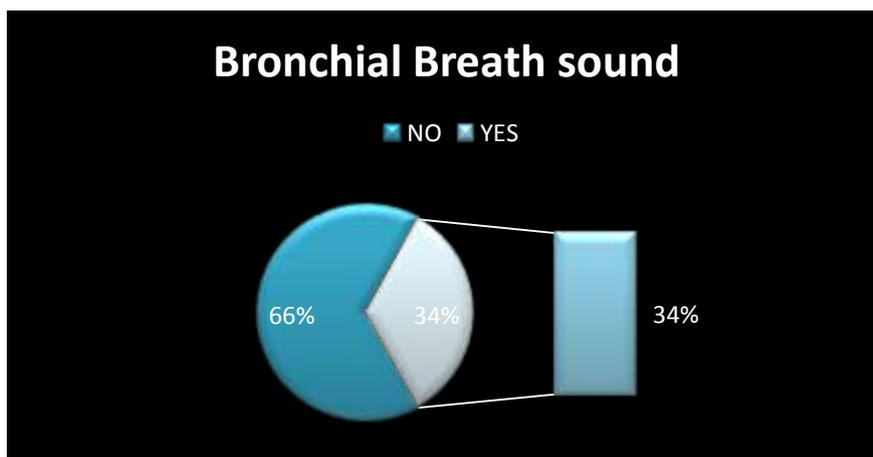
**Table.11.** Distribution of Wheeze

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



**Table.12.** Distribution of Bronchial Breath Sounds

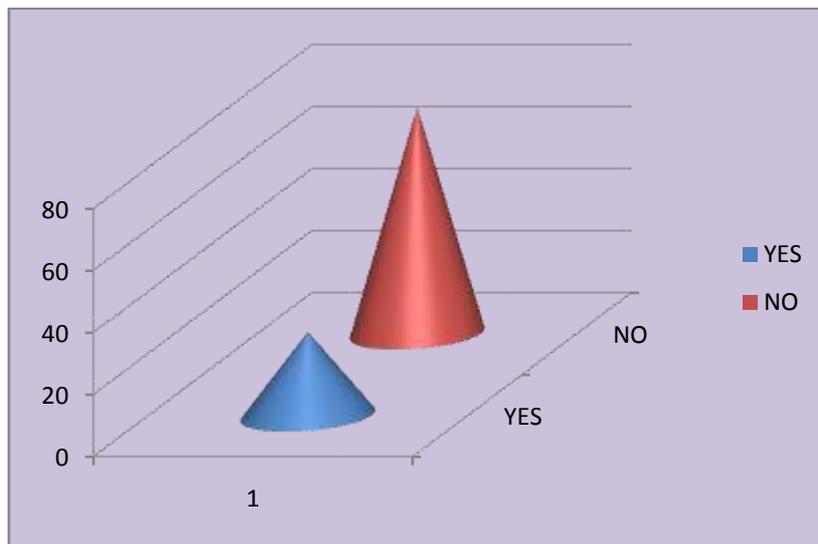
Bronchial Breath Sounds	Frequency	Percent
NO	66	66.0
YES	34	34.0
Total	100	100.0



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 crepitaions
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

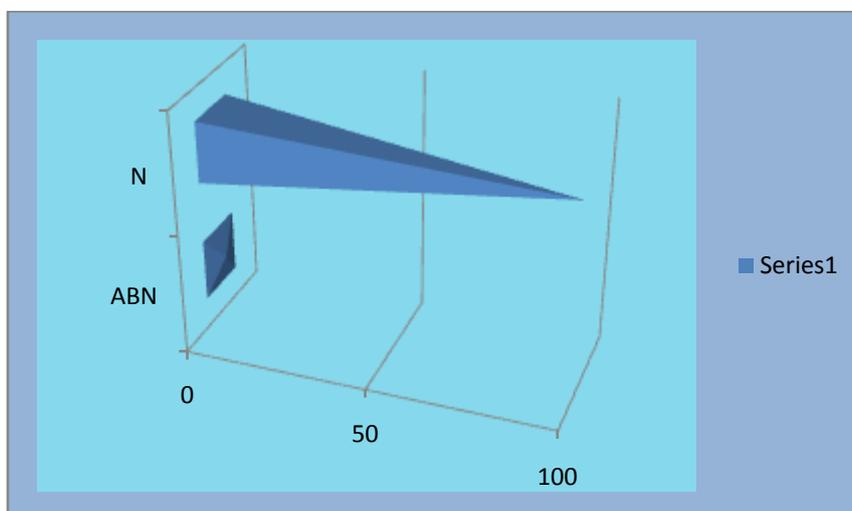
**Table.13.** Distribution of Anaemia

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



**Table.14.** Distribution of Bilirubin

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



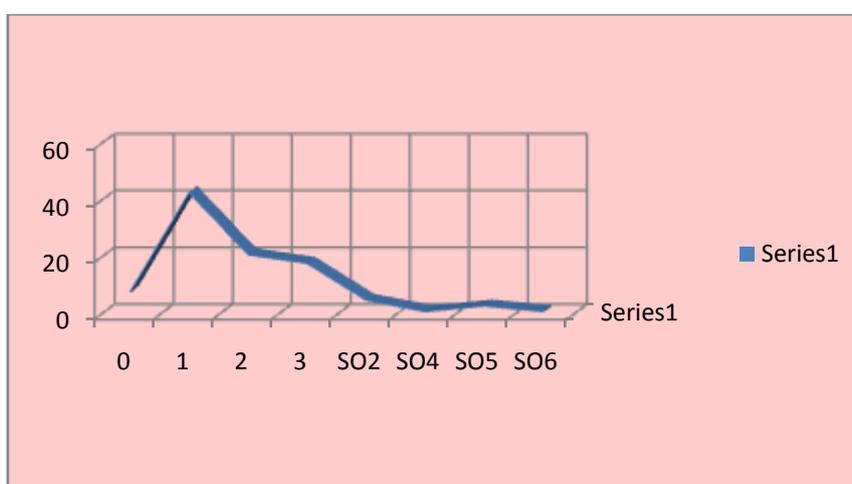
**Table.15.** Distribution of SGOT and SGPT

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



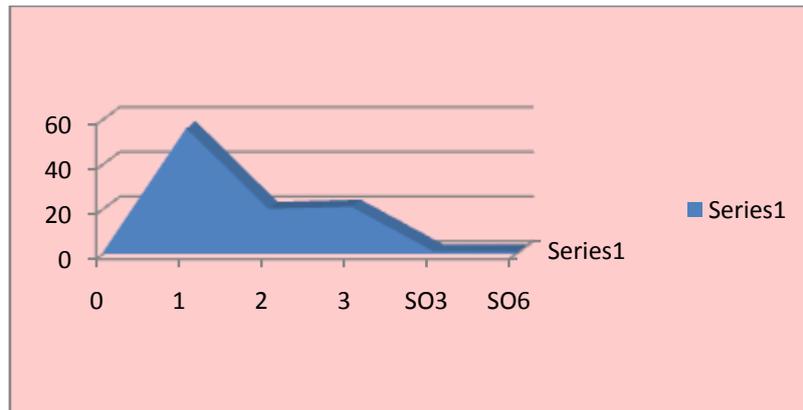
**Table.16.** Distribution of Sputum A sample

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.17.** 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 RaisedS.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.18. 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

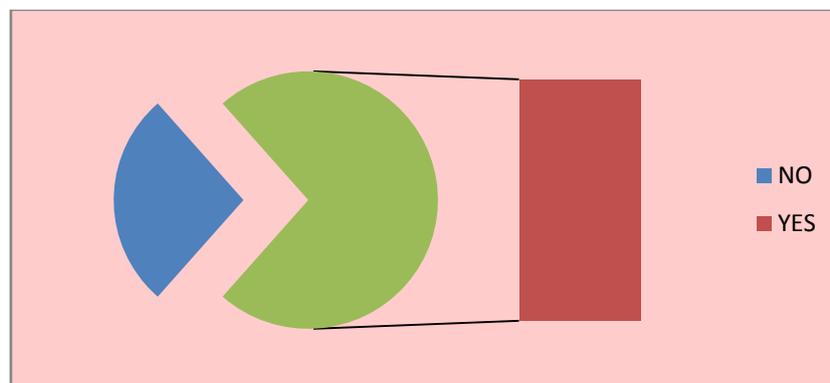
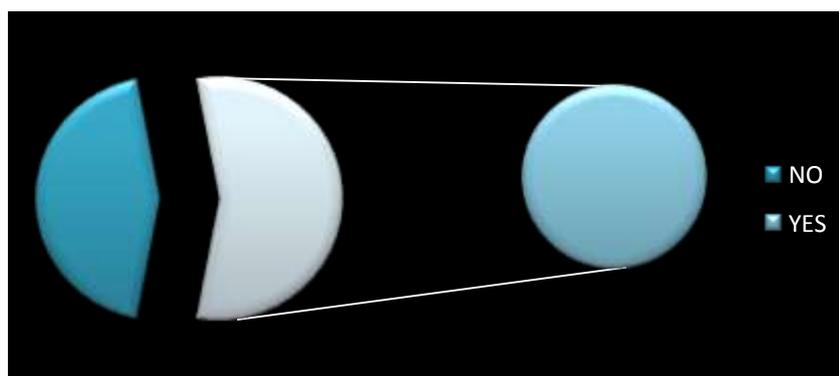


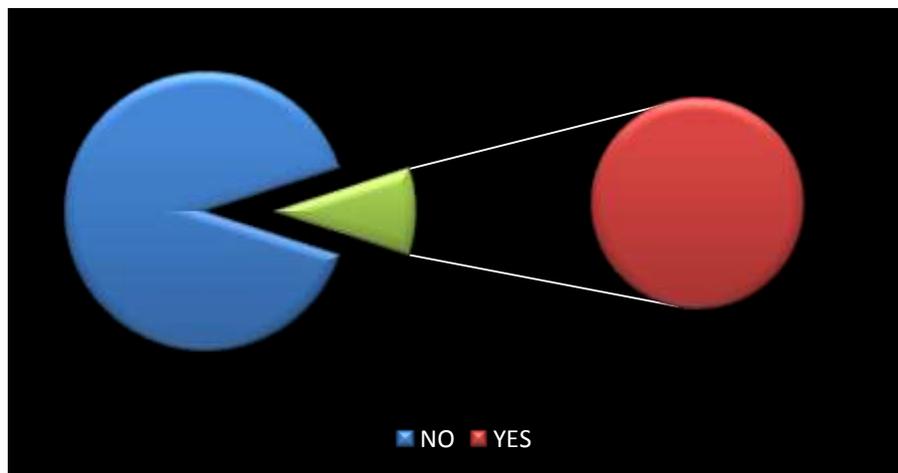
Table.19. Distribution of Mid Zone Infiltration in Chest Xray

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



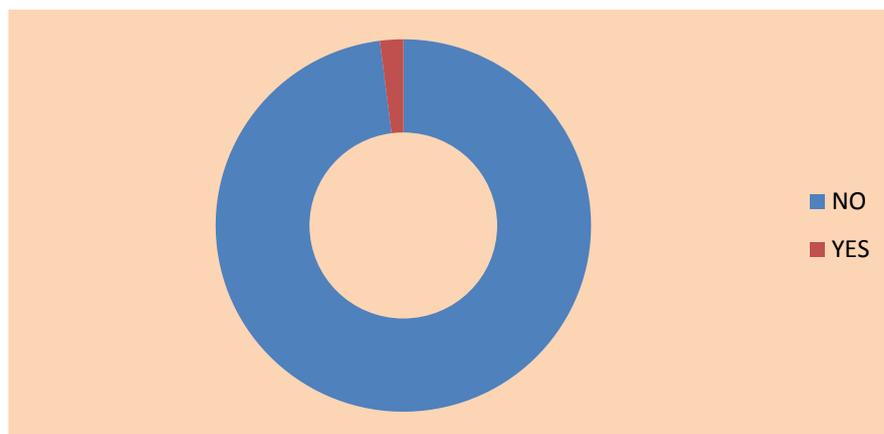
**Table.20.** Distribution of Lower Zone Infiltration in Chest Xray

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



**Table.21.** 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. In 10 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.

#### IV. 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 laborers 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 anemia 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.22** comparison of symptoms between this study and study by bikaram singh datta et al.

Symptoms	Present Study (%)	Bikaram Singh Datta et al (%)
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 bikaramsingh study. Like wise 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 Pradesh 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 OfMdr-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%.

## V. 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 indicator 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.

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