

A RETROSPECTIVE STUDY ON MULTI DRUG RESISTANT TUBERCULOSIS IN A TERTIARY CARE HOSPITAL: AN ALARMING THREAT OF CONCERN.

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Abstract

Introduction:

MDR-TB is becoming a significant global health concern in this era. Globally, the incidence of MDR-TB is 3.4% in new cases and 18% in previously treated cases. MDR-TB mostly arises due to inadequate treatment, poor compliance to drugs, and/or direct contact with a MDR-TB patient and hence is essentially a man-made phenomenon. The prevalence of MDR-TB in any area is mirrored by the functional state and efficiency of tuberculosis control programs running in the country.

Material and Method:

A total of 549 cases were recruited during the period from 2017 to 2019 and the data were analyzed retrospectively. Both pulmonary and extra-pulmonary samples were collected with proper aseptic measures. Direct microscopy by Ziehl Neelsen (ZN) staining was done. Further liquid culture and first-line drug susceptibility testing were performed in MGIT 960.

Result:

Out of 549 enrolled cases, 312 Mycobacterium tuberculosis cases were confirmed. The prevalence of mono or multi-drug resistance of MTB patients to 1st line drugs during 2017, 2018, and 2019 were 51.7%, 52.1%, and 49.1% respectively. The present study showed a prevalence of MDR-TB in new cases and of previously treated TB cases on an average of 2.7% and 11.2% which is slightly lower than the national level data of 3.4% and 18% respectively.

Conclusion:

India is showing an increased prevalence of MDR-TB which leads to the greatest obstacle to the End TB strategy adopted by the WHO and the government of India. There is an urgent need for continuous surveillance of MDR-TB. A Retrospective study on

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1. Introduction:

Every year, tuberculosis (TB) infects millions of people, representing an alarming threat as a major health challenge leading to one of the impor-

tant causes of death worldwide. Approximately 10.6 million people were estimated to be affected by TB in 2021 globally with an increase in incidence rate by 3.6%, which is equivalent to 134 cases per 100000 population. [i] The overall increase in TB incidence is estimated to have occurred as a result of the impact of the COVID-19 pandemic on TB detection during 2020 and

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2021. Geographically, most TB cases in 2021 were in South-East Asia (45%), Africa (23%), and Western Pacific (18%), followed by Eastern Mediterranean (8.1%), America (2.9%), and Europe (2.2%).¹ In 2021, there were an estimated 1.6 million deaths, the majority of which are in resource-limited countries.¹ Multidrug-resistant tuberculosis (MDR-TB) is defined as resistance to at least isoniazid and rifampicin, with or without resistance to other anti-TB drugs. [ii] Emergence of MDR-TB is becoming a significant global health concern in this era, and as in 2021,¹ globally there were an estimated 5 lakhs incident cases of MDR-TB with 3.1% increase in incidence and 2 lakhs cases of death due to MDR. [iii], [iv] The global incidence of MDR-TB is 3.4% in new cases and 18% in previously treated cases. Since 1994, the World Health Organization (WHO) has systematically collected and analyzed data on levels of resistance to anti-TB drugs from many countries and territories. [v] The alarming reports of drug resistance are on the increase from major parts of the globe resulting in disruption of the gains achieved in tuberculosis (TB) control over last few decades. [vi] MDR-TB mostly arises due to inadequate treatment, poor compliance to drugs or direct contact with a MDR-TB patient and hence is essentially a man-made phenomenon, [vii], [viii] The prevalence of MDR-TB in any area is mirrored by the functional state and efficiency of tuberculosis control programs running in the country. Many risk factors for the development of resistance to TB have been described by the World Health Organization. [ix] Numerous studies have established many risk factors associated with MDR-TB which include poor adherence to treatment, improper dosage, a short duration of treatment and inadequate drugs. [x] Similarly, a case-control study conducted in Ethiopia identified a history of TB treatment as a main determinant of MDR-TB. [xi] Hence, India is facing a big challenge on completion of treatment and cure from MDR-TB. [xii] The present study focuses on the prevalence of MDR-TB and pattern of drug resistance among suspected tuberculosis patients from a tertiary care center in Northern India.

2. Material and Methods:

The present study was a retrospective cross-sectional study of the north-eastern region of a three-year duration. Both pulmonary and extrapulmonary samples were received from the outpatient department of the Chest and TB clinic at Rajendra Institute of Medical Sciences, Ranchi, Jharkand, India. A total of 549 cases were recruited during the period from 2017 to 2019 and the data were analyzed retrospectively. Both pulmonary and extrapulmonary samples were collected with proper aseptic measures and sent to our lab without delay for immediate processing. Early morning sputum sample was preferred in a sterile wide-mouthed container as per the guidelines described in the Revised National TB Control Programme. Common extrapulmonary samples such as pus, CSF, synovial aspirate, ascitic fluid, pleural fluid, and endometrial tissue were obtained from presumptive TB cases. Direct microscopy by Ziehl Neelsen (ZN) staining was done for detecting AFB bacilli in all samples as a preliminary test. Further, specimens were decontaminated and concentrated using NALC-NAOH solution and all specimens were processed for liquid cultured in BACTEC MGIT 960. 500 μ L of the specimen was inoculated into MGIT tube containing 7 ml of modified Middlebrook-7H9 broth. The MGIT 960 tube was enriched with supplements and antibiotics (PANTA) prior to inoculation. Cultures were incubated at 37°C for up to 42 days. Positive samples detected by the machine were further processed by ZN staining for detecting AFB bacilli. Differentiation and confirmation of Mycobacterium Tuberculosis (MTB) bacilli with atypical mycobacterium or Mycobacterium other than TB (MOTT) bacilli were further done by rapid immune-chromatographic test kit using MPT 64 antigen (ID Strip test kit) of MTB isolates.

MTB isolates were further processed in MGIT 960 for drug susceptibility testing of first-line drugs using Isoniazid (H), Rifampicin (R), Ethambutol (E), Streptomycin (S), and Pyrazinamide (Z).

3. Results:

A total of 549 specimens were tested and analyzed in the Department of Microbiology with 452 (82.3%) sputum samples and 97 (17.7%) extrapulmonary samples during three years of study duration. All specimens were examined for ZN staining showing acid-fast bacilli in 33.4% of cases. Among 549 cases, a total of 328 cases were growth positive comprising 90.2% sputum positive and 9.8% extrapulmonary cases. Further, the ID strip test kit confirmed 312 MTB and 16 MOTT cases. The age of patients ranged from 5 years to 70 years with the mean age of patients diagnosed with MTB being 32 years. The maximum no. of cases was found to be in the third decade of life (21-30) years, comprising 41.23% of the total cases. Male to female ratio among them was 2.18:1 with males being 68.6% and females 31.4%. Apart from these, other demographic characteristics and resistance patterns of MTB patients are depicted in Table 1. The prevalence of mono or multi-drug resistance of MTB patients to 1st line drugs during 2017, 2018, and 2019 are 51.7%, 52.1%, and 49.1% respectively as in Table 2. MDR TB (HR resistance) prevalence is 25.3%, 19.4%, and 18.9% for 2017, 2018, and 2019 respectively as depicted in Figure-1. The total prevalence of MDR in new TB cases is 2.7%, 2.6%, and 2.9%, and in previously treated cases are 11.2%, 10.8% and 11.6% in years 2017, 2018, and 2019 respectively shown in figure 2.

4. Discussion:

More than 2/3rd of patients were male and the mean age was 32 years. A study from Ahmedabad, showed 68.5% were males and 83.7% of patients were in the reproductive age group of 16-45 years with a mean age of 33.6±11.03. [i] More than 3/4th of patients were from rural areas and 63.5% were illiterate denoting decreased availability of healthcare facilities at the peripheral level as well as decreased awareness about signs and symptoms of disease. Majority of 71.8% patients belonged to a Joint family signifying rapid transmission among the contacts of family members. These results are consistent with other reported

findings. [ii],[iii],[iv] Most of the MTB patients were living in poor and unhygienic environmental conditions as evidenced by 61.5% of cases of overcrowding among symptomatic cases. A history of smoking was seen in 45.8% of cases indicating a predisposing factor for pathological changes in the lung. Nearly 90.2% of TB patients are of pulmonary origin and the rest involve other systems. In the present study, 49% of cases showed sensitivity towards all drugs and among the rest, Isoniazid and rifampicin showed maximum resistance of 40.8% followed by 30.8%, 22.1%, 3.1%, 1.8% resistance to Isoniazid, Rifampicin, Streptomycin, and Ethambutol respectively. This finding was consistent with studies on resistance patterns done by other authors with 49% of cases resistant to Isoniazid,[v] and with 29% and 34.07% resistant to Rifampicin. [vi] In the present study all cases showed sensitivity toward pyrazinamide drug. This is concerning other studies that demonstrated a low proportion of resistance to pyrazinamide (1.16%) ethambutol (1.74%) and streptomycin (1.74%).¹⁶ The current study showed a prevalence of MDR-TB in new cases and of previously treated TB cases on an average of 2.7% and 11.2% from three-year data which is slightly lower than national level data of 3.4% and 18% respectively. The low rate of MDR-TB in new patients is mostly due to their sensitivity to first-line drugs and the high rate in previously treated patients indicates secondary resistance due to inappropriate dosing, compliance to drugs, duration, and variability in the prescription of anti-tubercular drugs by clinician. [vii],[viii] Moreover, previously intermittent therapy under Directly Observed Treatment Short Course (DOTS) strategy also led to increase in resistance hence this has now been shifted to daily therapy under new RNTCP guidelines. [ix][20]

5. Conclusion:

India is showing an increased prevalence of MDR-TB which leads to the greatest obstacle to the End TB strategy adopted by the WHO and the government of India. There is an urgent need

Table 1: Demographic and resistant characteristics of MTB patients enrolled in this study (n=312)

Characteristic	Frequency (%)	95% CI
Age(Years)	91 (29.2%) 188	22.1-34.6
5-25	(60.3%) 33 (28.2%)	58.3-67.5
26-50		25.3-36.7
50		
Residence Area	219 (70.2%) 93	66.2-74.1
Rural	(29.8%)	24.8-34.5
Urban		
Sex	214 (68.6%) 98	61.3-72.4
Male	(31.4%)	26.6-34.8
Female		
Education	198 (63.5%) 114	56.8-65.4
Illiterate	(36.5%)	31.2-40.4
Literate		
Type of Family	88 (28.2%) 224	24.2- 35.6
Nuclear	(71.8%)	67.5-75.1
Joint		
Overcrowding housing condition Present	192 (61.5%) 120	56.3-66.8
Absent	(38.5%)	32.6-43.2
Smoking History	143 (45.8%) 169	39.1-51.7
Past	(54.2%)	48.7-57.6
Never		
Patient presenting as New Case Previously Treated case	247(79.2%) 65	71.4-84.5
	(20.8%)	15.3-28.6
Resistance pattern (n=159)	49 (30.8%)	24.2-36.1
H mono-resistant	35 (22.1%)	18.8-24.3
R mono-resistant	65 (40.8%)	36.3-45.6
H and R resistant	3 (1.8%)	0.6-5.2
H, R and E resistant	5 (3.1%)	2.6-9.7
H, R and S resistant	2 (1.3%)	0.3-4.5
H, R, S and E resistant		

Table 2: TB cases showing Sensitive and Resistant pattern from 2017-2019

Year (n=312)	Sensitive to all 1 st line Drugs (%)	MDR/Monoresistance to 1 st line drugs (%)	Significance level (P value)
2017 (n=87)	42 (48.3%)	45 (51.7%)	<0.05
2018 (n=98)	47 (47.9%)	51 (52.1%)	<0.05
2019 (n=127)	64 (50.4%)	63 (49.6%)	<0.05
Total n= 312	153 (49%)	159 (50.9%)	<0.05

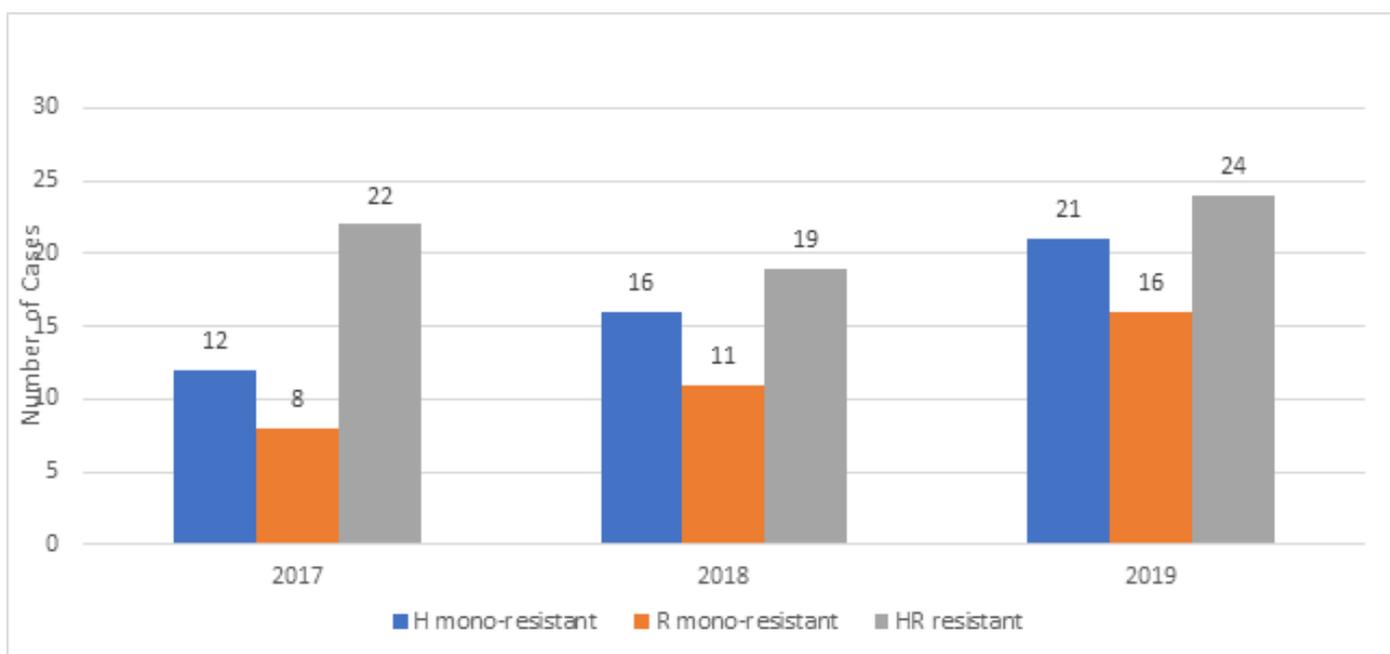


Figure 1: Temporal profile of TB drug resistant during 2017-2019

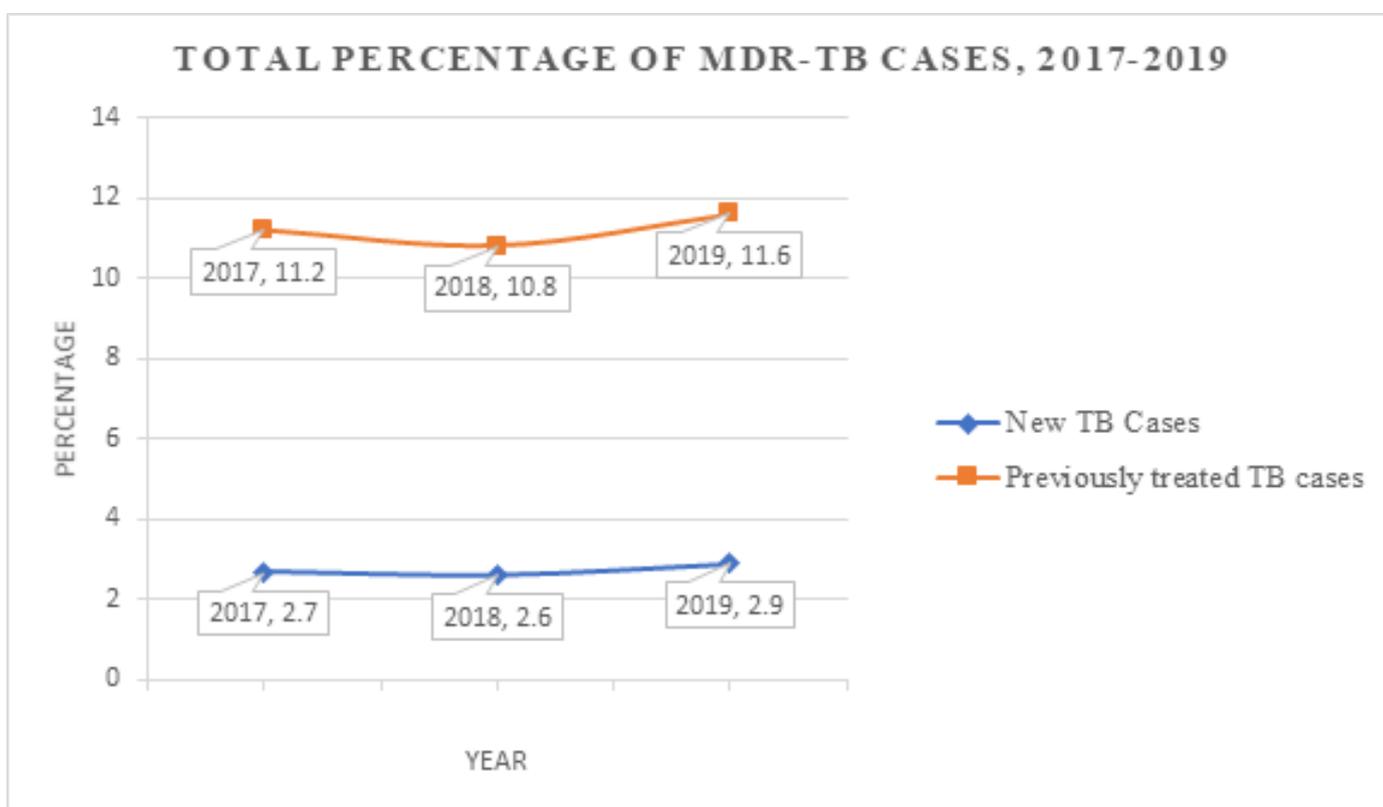


Figure 2: Total Percentage of MDR cases in new and previously treated TB patients

for continuous surveillance of MDR-TB. The latest concern of this era to decrease MDR-TB is by increasing awareness and repeated training of staff of primary care physicians and primary health center (PHC) as a priority related to the latest guidelines on MDR-TB.

6. The limitation of my study:

Is that Second line drug susceptibility was not performed at our setup due to limited resources and only three-year data were analyzed due to Covid -19 pandemic in succeeding years.

7. Conflict of Interest:

None

8. Funding

Nil

9. Abbreviations

ZN- Ziehl Neelsen
MTB- Mycobacterium Tuberculosis
DOTS- Directly Observed Treatment Short Course
H- Isoniazid
R- Rifampicin
E- Ethambutol
S- Streptomycin
Z- Pyrazinamide

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