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Prevalence of Multidrug Resistance Tuberculosis in Presumptive Multidrug Resistant Tuberculosis Cases Attending Tertiary Care Center

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ABSTRACT :

Background-The emergence of resistance to drugs used to treat tuberculosis (TB), and particularly multidrug-resistant TB (MDR-TB), has become a significant public health problem in a number of countries and an obstacle to effective TB control. In our study we tried to comprehend the prevalence of MDR TB in new cases and retreatment cases in suspected MDR cases in the department of pulmonary medicine MGM medical college and hospital Aurangabad, India.

Methods- A prospective observational study was conducted between January 2015 and March 2016 at department of pulmonary medicine. all the sputum samples were sent to Government medical college Aurangabad where they were examined for AFB by direct microscopy after homogenization and concentration by Petroffs method and staining by Ziehl-Neelsen method. The specimens were subjected culture and sensitivity for M.Tuberculosis. Culture was performed on LJ Media and sensitivity was done for Rifampicin and Isoniazid .On the bases of Sensitivity patients were labeled as MDR/Mono resistance or Non MDR.

Results- A total of 181 MDR suspects selected for the study .Patients were divided into 2 groups New cases and Retreatment cases which shows the prevalence of MDR is high in retreatment cases around 15.85 % when compared to New cases which is around 11.36 %. Mono resistance to INH was found to be 3.17%.

Conclusion- Our study was conducted in a small number but which clearly states the levels of MDR in new cases was high when compared to the WHO global estimate 2014 of MDR in new and previously treated cases .This show there is a almost need to improve our diagnostic modalities and good treatment plans to reduce the prevalence of MDR both new and retreatment cases. Subjecting new cases for first line drug sensitivity testing should be implemented. Our study emphasize the need of first line drug sensitivity testing in all the new cases of Tuberculosis.

Key words- MDR , XDR, PMDT ,WHO , DMC,TB

INTRODUCTION : Multidrug-resistant TB (MDR-TB), has become a significant public health problem in a number of countries and an obstacle to effective TB control. In India, the available information from the several drug resistance surveillance studies conducted in the past suggest that the rate of MDR-TB is relatively low in India. However this translates into a large absolute number of cases and as yet the management of patients with MDR-TB is inadequate. It is well known that poor treatment practices breed drug resistance. Areas with a poor TB control tend to have higher rates of drug resistant TB. It has been acknowledged that good

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treatment is a pre-requisite to the prevention of emergence of resistance. Prevention of emergence of MDR-TB in the community is more imperative rather than its treatment. It is impossible to tackle the problem of drug-resistant[1]

Drug-resistant TB has microbial, clinical, and programmatic causes. From a microbiological perspective, the resistance is caused by a genetic mutation that makes a drug ineffective against the mutant bacilli. An inadequate or poorly administered treatment regimen allows drug-resistant mutants to become the dominant strain in a patient infected with TB. [1] However it should be stressed that MDR-TB is a man-made phenomenon – poor treatment, poor drugs and poor adherence lead to the development of MDR-TB. [1] According to WHO Globally, an estimated 3.3% (95% CI: 2.2–4.4%) of new cases and 20% (95%CI: 14–27%) of previously treated cases have MDR-TB. In 2014, there were an estimated 480 000 (range: 360 000–600 000) new cases of MDR-TB worldwide, and approximately 190 000 (range: 120 000–260 000) deaths from MDR-TB. Among patients with pulmonary TB who were notified in 2014, an estimated 300 000 (range: 220 000–370 000) had MDR-TB. More than half of these patients were in India, China and the Russian Federation**.** [2]

In present study, we have estimated the prevalence of MDR-TB (defined as resistance to Rifampicin and Isoniazid with or without resistance to other drugs) in MDR- suspect patients attending the department of pulmonary medicine MGM Medical college and hospital Aurangabad, Maharashtra . These MDR-suspect patients (according to Guidelines on Programmatic Management of Drug Resistant TB (PMDT) in India may 2012) include any TB patient who fails an RNTCP category I or III treatment regimen, any RNTCP category II patient who is sputum smear positive at the end of the third month of treatment or later and close contacts of MDR-TB patients who are found to have smear positive pulmonary TB disease.

MATERIALS AND METHODS:

This study was a prospective observational study that involved all MDR-suspects attending the department of pulmonary medicine MGM Medical College and hospital Aurangabad, Maharashtra from January 2015 –March 2016.

DATA AND SPECIMEN COLLECTION-

Detailed history taken from patient. Patients were carefully inquired about their symptoms such as fever, cough, expectoration, chest pain, breathlessness, loss of appetite and loss of weight. Past history of anti tubercular drug intake was taken. Routine hematological investigations were requested for each patient including complete blood count, random blood sugar, liver function tests, kidney function tests, Elisa for HIV I & II and urine for routine-microscopy. A standard X-ray chest PA view was ordered for every patient.

Sputum for acid fast bacilli, smear microscopy, culture and drug susceptibility tests were performed at Department of Microbiology, Government Medical College Aurangabad. All sputa samples were first homogenized and concentrated by Petroff's method (modified) in GMC. Drug susceptibility testing was carried out by 'Minimal Inhibitory Concentration' method. Standard reference strain 'H37Rv' was tested additionally for comparability and precision Pt were divided into two groups.

Group A which included new cases of pulmonary tuberculosis [who never had tuberculosis in the past and was never exposed to any of the ATT drugs] who's sputum was positive after completion of 2 mouths of ATT which include $2H_3\ R_3Z_3E_3$.

Group B which include all treatment failure, relapse and treatment default cases [who had been exposed to anti tubercular drugs in the past] of cat I and cat II under RNTCP India who's sputum turned out to be positive for acid fast bacilli again.

INCLUSION CRITERIA –new cases of pulmonary tuberculosis who's sputum was

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positive after completion of 2 months of ATT All treatment failure, relapse and treatment default cases who had been exposed to ATT earlier and turned sputum positive for acid fast bacilli.

EXCLUSION CRITERIA-smear negative pulmonary tuberculosis MDR Treatment failure: MDR Treatment default: patients Still on MDR treatment:

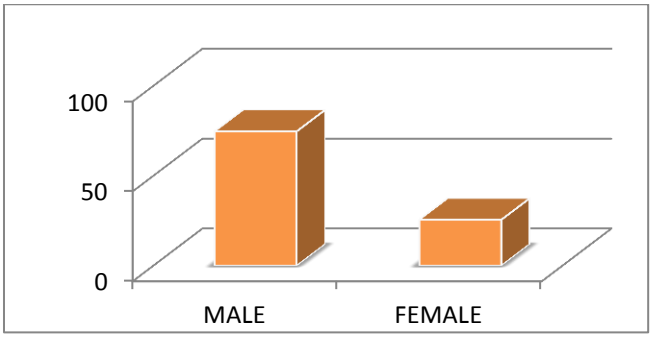
DRUG SUSCEPTIBILITY TESTING

Early morning sputum samples from patients were processed by the modified Petroff's method [3], stained by Ziehl-Neelsen Carbol Fuchsin, microscopically examined and cultured on Lowenstein-Jensen slopes (Himedia, India) as well as in Dubos broth (Himedia, India). Culture-negative or contaminated samples were excluded from the analysis. Biochemical tests for niacin and catalase production were performed to confirm the identity of *Mycobacterium tuberculosis*. Drug susceptibility testing of the samples was performed by the radiorespirometric Buddemeyer technique (a manual modification of the Bactec 460 technique) [4,5]. Briefly, samples were inoculated into Dubos broth containing ^{14}C Palmitic acid (Board of Radiation and Isotope Technology, India). Vials were set up in triplicate each containing 0.5×10^6/ml of Acid Fast Bacilli (AFBs) in absence (positive control) as well as presence of drugs (µgs/ml): Isoniazid (H – 0.1), Rifampicin (R – 2), Pyrazinamide (Z – 100) and Ethambutol (E – 2.5). Negative controls consisted of medium without acid fast bacilli (AFBs) as well as with heat killed AFBs. A 1:100 dilution of the positive control was also maintained. Readings were obtained daily until the eighth day in counts per minute (cpm) on a Wallac 1409 DSA liquid scintillation counter. Growth indices (GI) were calculated for the drug containing vials and the 1:100 positive control. Difference in growth indices (ΔGI), identical to that applied in the Bactec 460 method, calculated over consecutive days was used to determine susceptibility. The value of the mean ΔGI in the triplicate drug containing vials was compared to that for 1:100 control for the same day. If ΔGI was less in the drug containing vials than the 1:100 control, the bacteria were considered susceptible; if more, they were considered resistant [6,7].

Multidrug resistance (MDR) was defined as resistance to at least H and R. Other cases were categorized as follows: **Drug sensitive** – absence of resistance to any of the drugs, **monoresistance** – resistance to only 1 drug and **polyresistance** – resistance to at least two or more drugs excluding the HR combination.

RESULTS- A total of 184 MDR suspects patients selected for the study, out of which 58 patients were excluded from this study for various reasons. 126 patients were subjected for further evaluation in our study ,which included 94 male [74.60%] and 32 female [25.40%] patients .Patents were divided into 2 groups, Group A – [New Cases]Which had 44 patients from which 5 patients were MDR and 4 patients were detected with mono resistance to INH .The prevalence of MDR in New cases is around 11.36% and Group B – [Relapse/Retreatment]Which had 82 patients from which 13 patients were MDR which shows prevalence of MDR in Retreatment cases is 15.85 % and Out of 126 patients 3 patients were HIV Positive [2.38%].

SEX	FREQUENCY	PERCENT
MALE	94	74.60 %
FEMALE	32	25.40 %
TOTAL	126	100%



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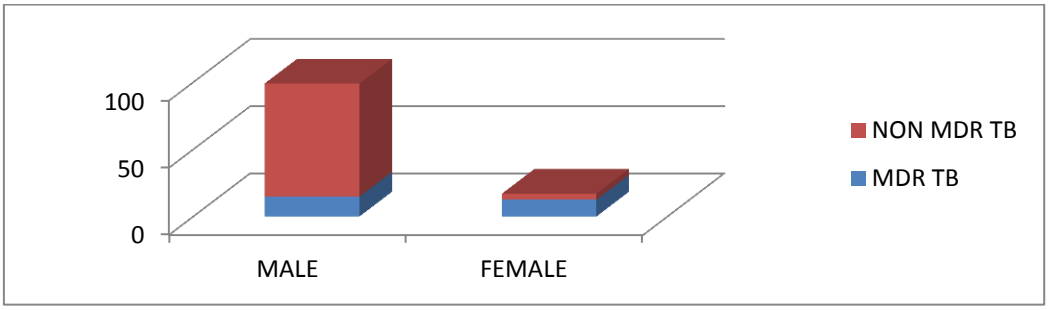
SEX	MDR TB	NON MDR TB	TOTAL
MALE	14 [14.89%]	80 [84.10%]	94 [100%]
FEMALE	4 [12.50%]	28 [87.50%]	32 [100%]
TOTAL	18 [14.28%]	108 [85.72%]	126 [100%]



GROUPS	A-NEW CASES	B- RELAPSE	TOTAL
MDR TB	05 [11.36%]	13 [15.85%]	18 [14.28%]
NON MDR TB	39 [88.64%]	69 [84.15%]	108 [85.72%]
TOTAL	44 [100%]	82 [100%]	126 [100%]

DISCUSSION

Drug-resistant TB poses a major threat to control of TB worldwide. By the end of 2014, data on anti-TB drug resistance were available for 153 countries, accounting for more than 95% of the world's population and estimated TB cases. Eighty of these countries have continuous surveillance systems, while the others rely on epidemiological surveys.

Extensively drug-resistant TB (XDR-TB) has been reported by 105 countries. On average, an estimated 9.7% (95% CI: 7.4–12%) of people with MDR-TB have XDR-TB.

There was major progress in coverage of drug susceptibility testing (DST) between 2013 and 2014. Worldwide, 12% of new bacteriologically-confirmed TB cases and 58% of previously treated TB patients were tested for drug resistance in 2014, up from 8.5% and 17% respectively in 2013 (representing proportional increases of 43% and 223%, respectively). Coverage was highest in the European Region (97% of new cases). In the South-East Asia and Western Pacific regions combined, two-thirds of previously treated cases underwent testing

Globally in 2014, 123 000 patients with MDR - TB or rifampicin resistant tuberculosis (RR-TB) were notified, of whom about 75% lived in the European Region, India, South Africa or China.

According to PMDT may 2012 the prevalence of MDR-TB in India to be about 3% in new cases and 12-17% in re-treatment cases. Study conducted at department of pulmonary medicine MGM hospital and medical college Aurangabad Maharashtra shows prevalence of MDR-TB in new cases is 10.52% and 16.25% in re-treatment cases

CONCLUSION

Our study shows that the prevalence of MDR TB is more in retreatment cases when compared to new cases, it should be emphasized that the prevalence of MDR TB in New cases is higher when compared to the values stated under PMDT

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2012 and WHO annual TB report 2015 .This is a threat to TB control Program in India [RNTCP] MDR TB diagnostic facility and surveillance activity should be expanded. Our study emphasize the need of first line drug sensitivity testing in all the new cases of Tuberculosis should be implemented to control, reduce the prevalence and improve the outcome of MDR TB treatment.

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