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Prevalence of Multi-Drug Resistant Tuberculosis among New Culture-Positive Pulmonary Tuberculosis Patients in Tertiary Care Center

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Keywords

MDR-TB, prevalence of MDR, Drug susceptibility, pulmonary tuberculosis;

Abstract

Increased "Multidrug-resistant" (MDR) strain prevalence is continuously becoming a significant public health concern as India is expected to eradicate tuberculosis (TB) by 2025. No prior use of anti-tuberculosis therapy (ATT) or use of ATT for less than one month was required for a new case of pulmonary tuberculosis (PTB). Two tertiary care referral institutions in North India gathered a single sputum sample from 380 probable PTB cases. All samples underwent Ziehl-Neelsen staining, "automated BACTEC MGIT 960" culture, and "Line Probe Assay" (LPA) drug susceptibility testing. In all patients with positive cultures, tests for Isoniazid and Rifampicin resistance were conducted.

There were 276 new PTB cases among the total of 380 patients (median age 28 years; 56.57% and 43.42% of whom were men and women, respectively). From these patients, 46 (16.66%) were rifampicin-resistant, 62(22.46%) were isoniazid-resistant, and 34(12.31%) were rifampicin- and isoniazid-resistant. New PTB cases have a high prevalence of MDR strains. Because centers served as referral institutions, there might be a higher prevalence.

1. Introduction

Tuberculosis (TB) is still a serious issue for world health. As per the records published by the "World Health Organization" (WHO), approximately 10.4m individuals was found with TB in 2016 and recorded 1.3 million death cases in the same year due to TB. 1 "Human Immunodeficiency Virus" (HIV) co-infection was the primary cause of the disease's mortality; 3.6 million patients passed away from HIV-TB coinfection. Rifampicin-Resistant TB (RRTB) cases increased by 0.6 million in 2016, with 0.5 million of those cases being MDR-TB. In India, along with the Russian Federation and China, 47% of these occurrences occurred [1]. Patients with MDR-TB, particularly those with pulmonary infections, present a significant public health risk because they have the potential to infect numerous close contacts with the strain. Additionally, the course of treatment for these patients can last up to 27 months and involves long-term injectable medications. Although successful, complete treatment includes a number of potentially fatal side effects and is greatly influenced by the patient's psychosocial surroundings. The intention to end this TB epidemic from the root area in the near future, early detection of TB patients and providing

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them proper treatment has become crucial. Calculating the frequency of MDR strains in newly cultured positive PTB cases was the main goal of this study.

2. Materials and Methods

Patients' recruitments

This particular study involved new PTB cases and was an observational one. New cases were those who had not previously had Anti-Tuberculosis Therapy (ATT) or had not received it in the previous month. After receiving prior written consent, all consecutive suspected PTB patients belong to the "Internal Medicine Outpatient Department" (IMOD) at the "All India Institute of Medical Sciences" in New Delhi and the "National Institute of Tuberculosis and Respiratory Diseases" in New Delhi during the years 2013 to 2016 were enrolled in the study. Before the study began, it received approval from the ethics committees of both institutes ("Ethical Clearance number, IEC/NP-62/2010"). Microbiological testing and the diagnosis of TB For each patient, a full blood count along with tests for liver and kidney function, as well as a chest X-ray, were performed. The sputum samples were decontaminated following the accepted decontamination procedure (Nacetyl-L-Cysteine-sodium hydroxide method). Ziehl-Neelsen (ZN) staining smear microscopy was performed on the pellet that was produced following decontamination [2]. Sputum samples that had been cleaned of contaminants were then utilised to inoculate "Lowenstein-Jensen" (LJ) medium and "BACTEC MGIT 960" (BD, Sparks, MD, USA) in form of liquid culture media [3].

The slow progression, colony morphology, inability to grow on L-J media that contains 500 g/ml of p-nitrobenzoic acid, catalase and niacin tests, as well as the immune-chromatographic test kit (considering-"SD MPT64TB Antigen detection" kit, Standard Diagnostics, Gyeonggi-do, South Korea) for liquid culture, were used to identify Mycobacterium tuberculosis. Using genotypic "Line Probe Assay" (LPA) and regarding phenotypic approaches, DST for first-line anti-TB medicines was performed on all culture-positive specimens (liquid or solid). A cost-effective adaptation of the 1% percentage approach was used to conduct drug susceptibility testing (DST) using LJ media [4]. A 40 g/ml drug concentration was used to test for drug susceptibility. Any strain with 1% (the critical proportion) or more of the "bacilli resistant" to the drug was classified as such.

3. Statistical analysis

STATA v12.2 was used for analyzing data ("StataCorp"- College Station, situated in Texas, United States of America). Mean and standard (SD) values were calculated for data those were distributed normally. On the other hand, range and median were calculated for data those did not follow a normal distribution.

4. Results

Out of the 380 patients were selected among which 215 (56.57%) were men and 165 (43.42%) were women. 28(10–80) years old was the average age. Table 1 provides baseline information. A total of 182 (47.89%) and 198 (52.10%) had positive and negative smear results, respectively, with 69/182 (37.9%) and 175/198 (88.38%) having positive results on the basis of the culture.

Table 1: Baseline demographic data.

Parameters	**Patients with Tb (n=380)**
Median Age (Range) in years	28 (10-80)
Male	215 (56.57%)
Female	165 (43.42%)
Smoking status	
Smoker	87 (22.89 %)
Past-smoker	104 (27.36%)
Non-smoker	136 (35.78%)

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Unknown	53(13.94%)
Blood investigations	
Hemoglobin (gm/dl)	10.4 ± 1.1
Platelet count (cells/ul)	146.7 ± 32.4
Erythrocyte sedimentation rate (mm in 1st hour	12.7 ± 2.3
Total lymphocyte count (cells/ul)	6.1 ± 1.7
Urea (mg/dl)	21.6 ± 10.3
Creatinine (mg/dl)	1.0 ± 0.2
Sodium (mmol/l)	127.9 ± 5.3
Potassium (mmol/l)	4.3 ± 0.5
Total Bilirubin (mg/dl)	0.37 ± 0.16
Total protein (gm/dl)	7.6 ± 1.4
Albumin (gm/dl)	4.5 ± 0.3

Among a total number of 296 patients, 276 new cases was there who had culture-positive results. The resistance rates for these 683 patients were as follows: 62(9.1%) for rifampicin, 75 (11%) for isoniazid, and 60 (8.7%) for both medications.

Table 2: Resistance prevalence

	Newly diagnosed patients; culture positive (n/N)	
	n/N	%
Any resistance to Rifampicin	46/276	16.66%
Any resistance to Isoniazid	62/276	22.46%
MDR-TB	34/276	12.31%

5. Discussion

India has been reported with the highest numbers of newly defined TB and MDR-TB cases worldwide and provides almost one-third of the global TB case burden [1]. Numerous studies have examined the prevalence of MDR-TB in India, finding that it ranges from 0.6% to 24% of all new TB cases [around 5 to 7]. The percentage of MDR TB patients who had previously consumed ATT ranged from 8% to 67% [8-11]. Despite the fact that these studies were carried out in various regions of India, they concur with overall data [1] in showing a growth pattern in the prevalence of MDR TB cases. According to a recently conducted meta-analysis, the prevalence of MDR-TB increased continuously. The estimation detected that from 4.1% of all new cases between 1995 and 2005 to 5.6% between 2006 and 2015. The vast majority of these research used culture as their DST method [12]. Some of the causes of rising resistance include an unsupervised as well as incomplete therapy, poor monitoring and misunderstandings about TB treatment, inadequate social support, improper nutrition and a poor political commitment level [1]. According to estimates, the incidence of MDR-TB in India could rise from the current rate of 3.9 cases per 100,000 people (Confidence Interval (CI) of 95%) to as high as 14.1 cases per 100,000 people (95% CI) if current TB treatment practises continue. The primary transmission incidents of an MDR strain would rise from 15% to 85% of all MDR cases, according to the same study's hypothesis [13]. The considerable variation in resistance prevalence across different regions of India points to the absence of national surveillance standards. The “Revised National

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Tuberculosis Programme" (RNTCP) carried out drug-resistance survey at national level for the first time that took place from 2014 to 2016 in recognition of this necessity [14]. It noted that among new PTB patients (n=3065), the prevalence of any isoniazid resistance and MDR strains was 11.6% and 2.84%, respectively. Isoniazid resistance was equally common in our sample, although MDR was nearly three times higher. This can be a result of referral bias brought on by the fact that our laboratory serves as a referral centre.

In countries with high TB burdens like India, where resources are scarce and the burden of both infectious and non-communicable diseases is rising, it is crucial to do such studies. Currently, approximately 30% of the target population in India receives MDR-TB treatment [1], and only 46% of those individuals were successfully treated in 2015. Twenty percent (20%) of MDR-TB patients who were receiving therapy died or were lost to follow-up [15]. The RNTCP released the "Programmatic management of Drug-Resistant TB (PMDT)" guidelines in 2017 [13] as a result of this being a significant issue that needed to be addressed. Our findings highlight the significance of maintaining a comprehensive surveillance programme for TB in order to track drug resistance trends in India and allocate resources in a way that targets drug-resistant TB.

6. Conclusion

MDR-TB is very common in newly diagnosed pulmonary TB patients. This outcome might not be efficiently descriptive of the population consisting general patient because both centers were tertiary care and referral facilities.

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