Journal of Tuberculosis and Therapeutics

Sinha et al., J Tuberc Ther 2018, 3:2

Research Article Open Access

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

Sanjeev Sinha[1*], Kartik Gupta[1], Mikashmi Kohli[1], VP Myneedu[2], RM Pandey[3] and PP Singh[4]

[1]*Department of Medicine, All India Institute of Medical Sciences, New Delhi, India*

[2]*National Institute of TB and Respiratory Diseases, New Delhi, India*

[3]*Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India*

[4]*NIPER, Mohali, Punjab, India*

[*]**Corresponding author:** Sanjeev Sinha, Department of Medicine, AIIMS, New Delhi, P.O. Box 110029, India, Tel: +919810164416; 011-26594440; Fax: 011-26588918; E-mail: drsanjeevsinha@gmail.com

Received Date: February 09, 2018; **Accepted Date:** March 30, 2018; **Published Date:** April 06, 2018

Abstract

Introduction: As India aims to end Tuberculosis (TB) by 2025, increased prevalence of Multi-Drug Resistant (MDR) strains continues to be a major public health concern.

Methods: New case of Pulmonary TB (PTB) was defined as no history of Anti-Tuberculosis Therapy (ATT) intake in the past or taken ATT for <1 month. Single sputum specimen from 1103 suspected PTB cases was collected at two tertiary care referral centers in North India. All samples were subjected to Ziehl-Neelsen stain, culture using automated BACTEC MGIT™ 960™ and Drug Susceptibility Testing using Line Probe Assay. Resistance testing for Rifampicin and Isoniazid was done in all culture-positive patients.

Results: Of the total 1103 patients (Median Age 34 years, 59% and 41% males and females respectively), there were 683 new PTB cases with liquid culture positive. From these patients, 62 (9.1%) were resistant to rifampicin, 75 were resistant to isoniazid (11%) and 60 (8.7%) patients were resistant to both drugs.

Conclusion: There is a high burden of MDR strains among new PTB cases. A higher prevalence could be because centers were referral institutes.

Keywords: MDR-TB; Pulmonary tuberculosis; Drug susceptibility

Introduction

Tuberculosis (TB) remains a major global health problem. In 2016, World health organization (WHO) estimated 10.4 million people developed TB and 1.3 million died from the disease.1 Mortality of the disease was predominantly observed in Human Immunodeficiency Virus (HIV) co-infection, 3.6 million patients died due to HIV-TB co-infection. In 2016, there were 0.6 million new Rifampicin-Resistant TB (RRTB) cases, of which around 0.5 million had Multi-Drug Resistant TB (MDR-TB). Almost half (47%) of these cases were in India, China and the Russian Federation [1].

MDR-TB patients, especially with pulmonary infection pose a great challenge to public health since they have the potential to spread the strain to many close contacts. In addition, treatment of these patients requires long-term injectable drugs and can extend up to 27 months. Complete treatment, though effective, has a myriad of life-threatening side effects and is dependent on a large part to the psycho-social environment of the patient. Detection and early-treatment of these patients become imperative if the goal of ending TB epidemic is to be realized anytime in the near future.

The primary objective of this study, therefore, was to calculate the prevalence of MDR strains in new culture positive PTB cases.

Materials and Methods

Patient recruitment

This was an observational study involving new cases of PTB. New cases were defined as those with no history of Anti-Tuberculosis Therapy (ATT) intake in the past or intake for <1 month. All consecutive suspected PTB patients during the period of 2013-2016 from the Internal Medicine Outpatient Department, All India Institute of Medical Sciences, New Delhi and National Institute of Tuberculosis and Respiratory Diseases, New Delhi were enrolled in the study after taking prior written consent. The ethics committee of both institutes gave approval before the study was started (Ethical Clearance number IEC/NP-62/2010).

TB diagnosis and microbiological tests

Complete blood count, Liver and Kidney function tests along with Chest X-Ray was done for all patients. The sputum specimens collected were decontaminated using standard decontamination protocol (N-acetyl-L-Cysteine-sodium hydroxide method). The pellet obtained after decontamination was used for Ziehl-Neelsen (ZN) staining smear microscopy [2]. Decontaminated sputum specimens were then used for culture inoculation on Lowenstein-Jensen (LJ) media and BACTEC MGIT™ 960™ (BD, Sparks, MD, USA) liquid culture media [3].

Mycobacterium tuberculosis was identified by slow growth rate, colony morphology, inability to grow on L-J media containing p-nitrobenzoic acid (500 µg/ml), niacin and catalase tests immuno-chromatographic test kit (SD MPT64TB Ag kit, Standard Diagnostics, Gyeonggi-do, South Korea) for liquid culture. All culture-positive specimens (liquid or solid) were further subjected to DST for first-line anti-TB drugs using genotypic [Line Probe Assay (LPA)] and phenotypic methods.

Drug susceptibility testing (DST) was carried out on LJ media by an economic variant of 1% proportion method [4]. Drug susceptibility was tested at a concentration of 40 µg/ml Any strain with 1% (critical proportion) of bacilli resistant to the drugs was classified as resistant to the drug.

Statistical analysis

Data were analyzed using STATA v12.2 (StataCorp, College Station, Texas, USA). Mean and SD was calculated for data following normal distribution while median and range were calculated for data not normally distributed.

Results

Out of 1103 patients recruited, there were 649 (59%) males and 454 (41%) females. The median age was 34 (10- 80) years. Baseline data is given in Table 1. A total of 508 (46.1%) and 595 (53.9%) were smear-negative and positive respectively, of which 166/508 (32.7%) and 547/595 (95.9%) were culture positive, respectively.

Parameter	TB patients (n=1103)
Median Age (Range) in years	34 (10-80)
Male	649 (59%)
Female	454 (41%)
Smoking status	
Smoker	117 (11%)
Past smoker	314 (28%)
Non-smoker-	584 (53%)
Unknown	93 (8%)
Blood investigations	
Hemoglobin (gm/dl)	12.3 ± 1.2
Platelet count (cells/ul)	167.7 ± 36.3
Erythrocyte sedimentation rate (mm in 1st hour	14.9 ± 2.5
Total lymphocyte count (cells/ul)	6.3 ± 1.8
Urea (mg/dl)	22.8 ± 10.4
Creatinine (mg/dl)	1.0 ± 0.3
Sodium (mmol/l)	139.7 ± 6.6
Potassium (mmol/l)	4.4 ± 0.4
Total Bilirubin (mg/dl)	0.39 ± 0.18
Total protein (gm/dl)	7.7 ± 1.6
Albumin (gm/dl)	4.7 ± 0.4
Aspartate aminotransferase (SGOT) (IU/l)	36.4 ± 7.4
Alanine aminotransferase (SGPT) (IU/l)	34.3 ± 9.8
Alkaline phosphatase (ALP) (IU/l)	133.3 ± 44.3
Data are presented as median, range; mean ± SD or absolute number (%)	

Table 1: Baseline demographic data.

From a total of 713 patients with culture-positive results, there were a total of 683 new cases. Of these 683 patients, 62 (9.1%) were resistant to Rifampicin, 75 (11%) were resistant to Isoniazid and 60 (8.7%) patients were resistant to both drugs (Table 2).

	Newly diagnosed patients; culture positive(n/N)	
	n/N	%
Any resistance to Rifampicin	62/683	9.10%
Any resistance to Isoniazid	75/683	11%
MDR-TB	60/683	8.70%

Table 2: Resistance prevalence.

Discussion

India contributes nearly one third to the total TB case burden and has the highest number of new reported TB and MDR-TB cases in the world [1]. There have been various studies reporting the prevalence of MDR-TB in India with a range of 0.6% to 24% MDR-TB in new TB cases [5-7]. The proportion of MDR TB patients with the history of intake of ATT in the past varied from 8% to 67% [8-11]. Though these studies have been conducted in different parts of India, they indicate an increasing prevalence of MDR TB cases, in agreement with global data [1]. A recent meta-analysis showed that prevalence of MDR-TB has increased from 4.1% of total new cases in 1995-2005 to 5.6% cases in 2006-2015. Majority of these studies had used culture as the technique for DST [12]. Incomplete and unsupervised treatment, poor follow up and misconceptions about TB treatment, poor nutrition and social support, lack of political commitment are some of the reasons responsible for increasing resistance [1]. With the current practices of TB treatment in India, it is estimated that incidence of MDR-TB could increase from 3.9 cases/100 000 population [95% Confidence Interval (CI)] currently to as high as 14.1 cases/100 000 population (95% CI 11.2-16). In the same study, it was hypothesized that the rate of primary transmission of MDR strain would increase from 15% to 85% of total MDR cases [13].

The wide range of resistance prevalence from different parts of India indicates the lack of uniform surveillance methodologies across the country. Realizing this necessity, the first national drug resistance survey was conducted by the Revised National Tuberculosis Programme (RNTCP) from 2014-2016 [14]. It recorded the prevalence of any Isoniazid resistance and MDR strains in new PTB cases (n=3065) to be 11.6% and 2.84% respectively. In our study, the prevalence of Isoniazid resistance was the same but MDR was almost three-times. This could be due to our laboratory being a referral center and subsequent referral bias.

Such studies are important to be done in high TB burden countries like India which have limited resources and are experiencing the increased burden of both communicable and non-communicable diseases. MDR-TB treatment reaches <30% of the target population in India currently [1], with successful treatment in only 46% of cases in 2015. One in every five (20%) patients on MDR-TB treatment died or was lost to follow up [15]. This has been a major issue needing addressal which led to RNTCP launching the Programmatic management of Drug-Resistant TB (PMDT) guidelines in 2017 [13].

Our findings emphasize the importance of continuing the systematic surveillance of TB to monitor the trends of drug resistance in India, with appropriate direction of resources to drug-resistant TB.

Conclusion

There is a high prevalence of MDR-TB in new pulmonary TB patients. Since both centers were tertiary care and referral institutes, this result might not be reflective of the general patient population.

Funding

We thank the Department of Pharmaceutical, Ministry of Chemical and Fertilizers, Government of India for funding this project.

Acknowledgement

We thank the staff members of DOTS center for their help during patient enrolment and follow-up. We acknowledge the support and coordination of the PhD students of the Department of Medicine.

References

1. WHO (2017) Global Tuberculosis Report. World Health Organization, Geneva.
2. Revised National Tuberculosis Control Programme Laboratory Network (2005) Guidelines for quality assurance of smear microscopy for diagnosing tuberculosis.
3. Siddiqi SH, Ruesch GS (2006) MGIT procedure manual for BACTECTM MGIT 960TM TB system.
4. http://www.who.int/tb/laboratory/mycobacteriology-laboratory-manual.pdf
5. Sharma SK, Kaushik G, Jha B, George N, Arora SK, et al. (2011) Prevalence of multidrug-resistant tuberculosis among newly diagnosed cases of sputum-positive pulmonary tuberculosis. Indian J Med Res 133: 308-311.
6. Jain NK, Chopra KK, Prasad G (1992) Initial and acquired isoniazid and rifampicin resistance to Mycobacterium tuberculosis and its implication for treatment. Indian J Tuberc 39: 12-14.
7. D'souza DT, Mistry NF, Vira TS, Dholakia Y, Hoffner S, et al. (2009) High levels of multidrug resistant tuberculosis in new and treatment-failure patients from the Revised National Tuberculosis Control Programme in an urban metropolis (Mumbai) in Western India. BMC Publ Health 9: 211.
8. Sharma SK, Kumar S, Saha PK, George N, Arora SK, et al. (2011) Prevalence of multidrug-resistant tuberculosis among Category II pulmonary tuberculosis patients. Indian J Med Res 133: 312-315.
9. Vijay S, Bala Sangameshwara VJ, Jagannatha PS, Kumar P (2004) Initial drug resistance among tuberculosis patients under DOTS Programme in Bangalore City. Indian J Tuberc 51: 17-21.
10. Shah AR, Agarwal SK, Shah KV (2002) Study of drug resistance in previously treated tuberculosis patients in Gujarat, India. Int J Tuberc Lung Dis 6: 1098-1101.
11. Hanif M, Malik S, Dhingra VK (2009) Acquired drug resistance pattern in tuberculosis cases at the State Tuberculosis Centre, Delhi, India. Int J Tuberc Lung Dis 13: 74-78.
12. Goyal V, Kadam V, Narang P, Singh V (2017) Prevalence of drug-resistant pulmonary tuberculosis in India: systematic review and meta-analysis. BMC Public Health 17: 817.
13. Law S, Piatek AS, Vincent C, Oxlade O, Menzies D (2017) Emergence of drug resistance in patients with tuberculosis cared for by the Indian health-care system: a dynamic modelling study. The Lancet Public Health 2: 47-55.
14. Revised National Tuberculosis Control Programme (2017) Guideline for PMDT in India 2017.
15. Central TB Division (2016) Revised National TB Control Programme Annual Status Report. Ministry of Health and Family Welfare, New Delhi.