Clinical Microbiology: Open Access
ISSN: 2327-5073

Pradhan et al., Clin Microbial 2013, 2:6
DOI: 10.4172/2327-5073.1000123

Research Article Open Access

Patterns of TB Drug-Resistance in a Tertiary Care Facility in Pune, India

Natasha Pradhan[1], Shailaja Desai[1], Anju Kagal[1], Sujata Dharmashale[1], Renu Bharadwaj[1],Shivahari Ghorpade[1], Sanjay Gaikwad[1], Vandana Kulkarni[2], Nikhil Gupte[2,3] Robert Bollinger[2,3], Amita Gupta[2,3] and Vidya Mave[2,3*]

[1]Byramjee-Jeejeebhoy Medical College, Pune, India
[2]Byramjee-Jeejeebhoy Medical College Clinical Trials Unit, Pune, India
[3]Johns Hopkins School of Medicine, Baltimore, Maryland, USA

Abstract

We aimed to evaluate the prevalence of MDR-TB among patients presenting with suspected MDR-TB to a tertiary care facility in Pune, India. We found 53% prevalence of MDR-TB among patients suspected to have MDR-TB. We also found XDR-TB pattern in seven cases. This finding at an urban government medical college might be useful for the country program to plan for advanced TB diagnostics and treatment facilities to curb the MDR-TB epidemic in India.

Keywords: Tuberculosis; Drug resistance; Resource-constrained setting; Prevalence

Introduction

Globally, the emergence of multi-drug resistant tuberculosis (MDR-TB) (defined as resistance to isoniazid (INH) and rifampicin (RIF) and extensively drug resistant (XDR-TB) (defined as resistance to INH, RIF, any fluoroquinolone and to at least one of the three injectable second line drugs-amikacin, kanamycin, capreomycin) has become a major challenge to effective TB control [1-4]. In 2008, of the estimated global annual incidence of 9.4 million TB cases, 1.98 million were estimated to have occurred in India. Among them, 131,000 were MDR-TB cases, representing 25% of the global MDR-TB burden [2,5].

Most hospitals including public hospitals in India do not have the necessary facilities to conduct routine testing for MDR- and XDR-TB. Yet these are the very places where many seek care and where there is particular risk for transmission to health care workers and to patients alike. Further, MDR-TB treatment comprisestoxic, expensive second-line drugs that have limited sterilizing capacity [6,7] resulting in poor treatment outcomes. Documenting the burden and antibiotic resistance patterns among patients suspected to have drug resistant TB is critical for patient management and for hospital resource allocation. Thus, the objective of our study was to evaluate the prevalence of MDR-TB and XDR-TB among patients presenting with suspected MDR-TB at our urban government medical college teaching hospital which caters to the city of >4 million people in Pune, India.

Materials and Methods

A retrospective review of microbiology records was performed at Byramjee-Jeejeebhoy Medical College-Sassoon General Hospitals (BJMC-SGH), Pune, Maharashtra. We extracted demographic data when available along with drug susceptibility testing (DST) information from accessible myco bacteriology laboratory records. The study included patients suspected to have MDR-TB who underwent TB culture and sensitivity between January 2008 and December 2010.All patients had been referred from BJMC chest clinic or hospital setting and had been suspected to have MDR-TB due to the following:-previously treated according to the revised national tuberculosis control programme (RNTCP) guidelines for TB; patients either had a persistently positive sputum for acid fast bacilli (AFB) or had not clinically responded by the end of three months of antitubercular treatment (ATT) [4].The BJMC institutional ethics committee and Johns Hopkins University institutional review board approvals were obtained.

Laboratory methods

All sputum and extrapulmonary specimens collected underwent digestion and decontamination using the NaOH-NALC method [8]. After centrifugation, the sediment was placed on smears for AFB staining. Approximately 10 microliters was then inoculated on Lowenstein-Jensen (LJ) slant and incubated. The slants were observed for growth weekly. If positive growth was identified, the isolates were further speciated by biochemical methods. The mycobacterial growth was further processed by proportion method for DST [9]. Sensitivity to first line drugs RIF, INH, ethambutol (EMB), streptomycin (STR) and to ciprofloxacin (CIP) and amikacin (AMK) was carried out in majority of the cases however CIP and AMK sensitivity was conducted instead of STR in 2008.

Statistical analysis

Analyses were performed using STATA, version 11.1. Logistic Regression analysis was performed to estimate the odds of association between MDR-TB and resistance to first and second line antitubercular medications. The level of significance was fixed at 5% for the analysis.

Results

During the 3 year study period, 13,173 patients were evaluated for suspected TB and 908 had culture confirmed TB cases. Of these, 249MDR-TB suspects underwent DST. Among the 249 MDR-TB suspects, 170(69%) were male and the median age was 34years. Two-hundred thirty one (98%) were pulmonary MDR-TB suspects (5 of whom were smear-negative) and 4(2%) were lymph node MDR-TB suspects.

DST of the 249 isolates revealed that 14(6%) were mono-resistant to INH, 23(9%) were mono-resistant to RIF, and 133(53%) were resistant

***Corresponding author:** Vidya Mave, Pathology Museum, 1st Floor, BJ Medical College, Pune, Maharashtra, India, Tel: (+91) 9503646148; E-mail: vidyamave@gmail.com

Received June 27, 2013; **Accepted** July 15, 2013; **Published** July 18, 2013

Citation: Pradhan N, Desai S, Kagal A, Dharmashale S, Bharadwaj R, et al. (2013) Patterns of TB Drug-Resistance in a Tertiary Care Facility in Pune, India. Clin Microbial 2: 123. doi: 10.4172/2327-5073.1000123

Anti-TB Drug Sensitivity	Overall n=249	2008 n=74	2009 n=70	2010 n=105
Any Resistance, n (%)				
RIF	170 (68)	59 (80)	44 (63)	67 (64)
INH	165 (67)	44 (59)	44 (63)	77 (73)
EMB	115 (47)	35 (47)	34 (49)	46 (44)
CIP	13 (20)	13 (18)	--	--
AMK	12 (19)	12 (16)	--	--
STR	94 (54)	--	29 (41)	65 (62)
Monoresistance, n(%)				
RIF	22 (13)	12 (20)	6 (14)	4 (6)
INH	14 (8)	0 (--)	5 (11)	9 (12)
EMB	6 (5)	2 (6)	3 (9)	1 (2)
CIP	0 (0)	0 (0)	--	--
AMK	0 (0)	0 (0)	--	--
STR	3 (3)	--	0 (0)	0 (0)
INH and RIF Resistant, n (%)	133 (53)	42 (57)	32 (46)	59 (56)
INH+RIF Only	16 (12)	7 (17)	3 (9)	6 (10)
INH+RIF+EMB	89 (67)	29 (69)	23 (72)	37 (63)
INH+RIF+CIP[1]	13 (31)	13 (31)	--	--
INH+RIF+AMK[1]	12 (29)	12 (29)	--	--
INH+RIF+STR	69 (76)	--	18 (56)	51 (86)
INH+RIF+EMB+STR	48 (53)	--	12 (38)	36 (61)
INH+RIF+CIP+AMK*[1]	7 (17)	7 (17)	--	--
INH+RIF+EMB+CIP+AMK[1]	5 (12)	5 (12)	--	--

Abbreviations: INH: Isoniazid; RIF: Rifampicin; EMB: Ethambutol; STR: Streptomycin; AMK : Amikacin; CIP: Ciprofloxacin; MDR-TB: Multidrug Resistant Tuberculosis(indicates resistance to at least INH and RIF); * denotes XDR-TB: Extensively Drug Resistant Tuberculosis(indicates resistance to isoniazid, rifampicin, ciprofloxacin and amikacin).

[1]CIP and AMK were only performed in 2008. Therefore XDR-TB could only be ascertained in 2008.

Table 1: Drug sensitivity patterns among patients undergoing TB culture-sensitivity between January 2008 and December 2010 in a tertiary care center, Pune, India.

to at least both RIF and INH indicating multidrug resistance (Table 1). Among 5 smear-negative pulmonary MDR-TB cases, 3(60%) were confirmed MDR. Among the 4 lymph node MTB cases, no multidrug resistance was detected. Neither mono-resistance to INH nor mono-resistance to RIF changed significantly over time though numbers of isolated were small. Resistance to at least both INH and RIF (i.e. MDR-TB) also did not change significantly over time. It was 57% (42/74) in 2008, 46%(32/70) in 2009 and 59% (59/105) in 2010 (p=0.31).

Among 133(53%) MDR-TB isolates, 16(12%) were INH and RIF resistant only, 89(67%)were INH/RIF/EMB resistant,13(31%) were INH/RIF/CIP resistant, 12(29%) were INH/RIF/AMK resistant, 69(76%) were INH/RIF/STR resistant, 48(53%) were INH/RIF/EMB/STR resistant, and 5(12%) were INH/RIF/EMB/CIP/AMK resistant (Table 1). In 2008, the only year CIP and AMK were tested, 7(5%) of 74 isolates were XDR-TB (defined as resistance to INH, RIF, CIP (flouroquinolone) and AMK (injectable).

Discussion

We observed that among MDR-TB suspects, who had culture-confirmed MTB and DST, 53% had MDR-TB and 6% and 11% had mono-resistance to INH and RIF, respectively. In addition, we found 7XDR-TB cases in the year when DST was performed for second line drugs amikacin and ciprofloxacin.

Globally, MDR-TB is on a rise and India is estimated to contribute a significant absolute burden of 25% [1-4]. Similar to our study, available data from tertiary care centers in India and from national reference laboratories show that 40 to 58% of MDR TB suspects are confirmed to have MDR-TB by DST. For example, a study from a tertiary care center in Vellore, India, found 58%isolates tested were MDR-TB [7] while two Mumbai tertiary care hospitals found 41-57% were MDR-TB [10,11].Likewise a study involving 13 Supranational Reference Laboratories (SRLs) representing 47 countries identified an MDR-TB prevalence of 39.4% among suspected MDR-TB cases [12].Our observed mono- resistance to INH and RIF was also comparable to other studies from tertiary care centers in India and other high TB burden countries[7,10-13].

Alarmingly, we found 5% of our MDR-TB suspects (7 cases) were XDR-TB in the one year we looked for it. XDR-TB has been reported in several countries in different regions of the world including India [3]. XDR-TB has been associated with very poor outcomes, with up to 50-80% of patients dying [6,7,14]. Identifying XDR cases in a very busy, crowded urban public hospital is of great public concern, particularly since most such settings lack the necessary capacity to identify such cases in a timely manner if at all. Beyond the very negative implications for the individual patient, most Indian public hospitals lack effective airborne infection control measures. Therefore there is substantial risk of transmission of this highly drug-resistant microbe in the health care setting [15-17]. Our study did not capture clinical outcome data of the MDR-TB or XDR-TB cases. We also were only able to assess for XDR-TB in one single year. However, our identification of the proportion of isolates that were drug-resistant and the ascertainment of specific patterns of drug resistance is useful for the country TB program to plan for emerging TB diagnostics particularly for detection of drug resistant strains such as Gene-Xpert and line probe assay and treatment facilities to curb the transmission of MDR-TB.

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