Assessment of extensively drug resistant tuberculosis by studying the drug sensitivity pattern in north Indian region

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**ABSTRACT**

Extensively drug-resistant tuberculosis (XDR-TB) is a form of TB caused by bacteria that are resistant to the most effective anti-TB drugs. The present study was carried out to demonstrate XDR prevalence in North Indian region. Out of 423 Mycobacterium tuberculosis cases, 166 had enough drug profile (i.e. resistant to Isoniazid and Rifampin plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., Amikacin, Kanamycin, or Capreomycin) to make or rule out a diagnosis of XDR. 85 out of 166 (51.2%) were Multiple Drug Resistance TB and 8 out of 166 (4.81%) were XDR cases.

**Keywords:** Extensively drug-resistant tuberculosis, Drug-susceptibility, Second-line drugs, p-Nitro-benzoic acid

**INTRODUCTION**

India has approximately two to three million people infected with Tuberculosis. In India, it is estimated that every year approximately 300000–350000 deaths are due to tuberculosis [1, 2]. Multidrug resistance tuberculosis have seen the widespread emergence of multidrug-resistant (MDR) tuberculosis, followed by extensively drug-resistant (XDR) tuberculosis and, most recently, strains that are resistant to all anti-tuberculosis drugs [3]. The tuberculosis control programs are severely threatened by drug resistance since it increases the possibility of a return to an era in which drugs are no longer effective. Numerous challenges have posed by XDR-TB in India, counting those of medical treatment and of TB control [4-6]. Worldwide a significant proportion of tuberculosis mortality is due to multi drug resistance (MDR) tuberculosis and some due to Extensively drug resistance (XDR) tuberculosis. Extensively drug-resistant tuberculosis (XDR-TB) is a form of TB caused by bacteria that are resistant to the most effective anti-TB drugs [7]. Some contend that XDR-TB strains have emerged from the mismanagement of multidrug-resistant TB (MDR-TB) and once created can spread from one person to another [8]. The exact nature of this mismanagement is not yet known, but origin of XDR-TB may coincide with the institution of new policies to promote drug compliance, such as DOTS. During the year 2008, there were associated with MDR-TB and approximately 50,000 cases of extensively drug resistant tuberculosis along with 30,000 deaths associated with XDR-TB. Drug resistant survey in several regions of India has found that about 3% new patient and 12-17 % of retreatment cases have MDR-TB, this criteria is higher than many other countries but much lower than hot spots described by WHO. XDR tuberculosis is defined as resistance to isoniazid and Rifampin and any one fluoroquinolone along with at least one of the three injectable second line drugs (i.e. amikacin, Kanamycin or shigh
mortality among persons infected with Human Immunodeficiency Virus (HIV) who are benefiting from antiretroviral therapy [9-11]. Given the tuberculosis and HIV epidemic in our country, Auroprobe Laboratories undertook the present multicentric study with most of the cases coming from Delhi and suburbs, to assess the presence of XDR TB.

**MATERIALS AND METHODS**

Only pulmonary specimens were considered for the current study & the Institutional Ethical clearance was taken. All the clinical specimens were decontaminated using Modified Petroff’s method (NaOH-NALC) and then cultured in BACTEC 12 B medium [12]. Periodical growth index (GI) readings were noted. All vials, which showed growth, were subjected to NAP (p-nitro-a acetylamino β hydroxypropiophenone) differentiation assay and MTB isolates were subjected to drug sensitivity assay using recommended MIC of different anti tuberculosis drugs. We collated our database from 2002 to 2006 and looked for cases satisfying the criteria for XDR TB. Only the cases with both TB culture and drug sensitivity done at Auroprobe Laboratories were included. The cases with only culture without drug sensitivity were excluded.

**RESULTS**

Out of total 621 cases of culture positive along with drug sensitivity profile for Mycobacterium species, 423 were *Mycobacterium tuberculosis*. Out of 423 *Mycobacterium tuberculosis* cases, 166 had enough drug profile (i.e. resistant to Isoniazid and Rifampin plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., Amikacin, Kenamycin, or Capreomycin) to make or rule out a diagnosis of XDR. 85 out of 166 (51.2 %) were MDR TB and 8 out of 166 (4.81%) were XDR.

**DISCUSSION**

MDR TB necessitates second line anti tuberculosis drugs, which are more toxic and expensive. XDR has emerged as a worldwide public health threat. According to a WHO report out of 20% MDR, 2% were XDR (with regional variations) [13-15]. In South Korea 14% of MDR cases were classified as XDR in years 2000-2004 while the figures for industrialized nations, Central and South America and Asia other than South Korea were11%, 4% and 3% respectively of all MDR cases. However these figures are based upon earlier definition of XDR, which was: resistance to Isoniazid and Rifampin and at least three of the six main classes of second-line drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicyclic acid). The criteria for XDR were subsequently changed because drug-susceptibility testing to fluoroquinolones and second-line injectable drugs (i.e., amikacin [aminoglycoside], Kenamycin [aminoglycoside], or Capreomycin [polypeptide]) yields reproducible and reliable results, whereas drug-susceptibility testing to other second-line drugs is less reliable [16]. Accordingly, the new agreed-upon definition of XDR TB is the occurrence of TB in persons whose *M. tuberculosis* isolates are resistant to Isoniazid and Rifampin plus resistant to any fluoroquinolone and at least one of three injectable second-line drugs (i.e., Amikacin, Kenamycin, or Capreomycin). Our study shows 4.8% XDR TB of all cases and 9.4% of all MDR cases have drug susceptibility pattern meeting the criteria for XDR.

**CONCLUSION**

The present study demonstrates that XDR is prevalent in India with possibly higher rates than reported in other studies performed in different regions of the world. Since approximately 10% of MDR cases were also XDR, we recommend that all MDR isolates should be subjected to second line drug susceptibility (at least one fluoroquinolone and all three injectable drugs), for better control of disease and preventing spread of these dangerous XDR strains in the community.

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REFERENCES