Journal of Infectious Diseases and Therapy
ISSN: 2332-0877

Vadthyavath and Muragundi, J Infect Dis Ther
2018, 6:3
DOI: 10.4172/2332-0877.1000365

Review article Open Access

Extensively Drug-Resistant Tuberculosis in India: Prevalence, Incidence and Burden

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Received date: May 3, 2018; **Accepted date:** May 26, 2018; **Published date:** May 31, 2018

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Abstract

Extensively Drug-Resistant Tuberculosis (XDR-TB) is a recent challenge for tuberculosis control program. The absence of the functional drugs and high rate of the failure in treatment and mortality rate also high jeopardize for epidemiology. Its prevalence is unknown in India as there was no nationwide counselling. Globally, there were an estimated 55,100 new extensively drug resistant tuberculosis cases in the year of 2015 in 117 countries. However, only 30 cases extensively drug-resistant tuberculosis was reported. Drug susceptibility test (DST) is the cornerstone to diagnose extensively drug resistant tuberculosis, but the lack of laboratory facilities in the resource-limited endemic countries limits its uses. A few new drugs including bedaquiline and delamanid have the potential to improve the efficiency of extensively drug-resistant tuberculosis treatment, but those drugs are used in 39 countries only. The costs of extensively drug resistant tuberculosis treatment (XDR-TB) are several folds higher than then multi drug-resistant tuberculosis (MDR-TB).

Keywords: XDR-TB; DST; MDR-TB; India

Introduction

The word extensively drug-resistant tuberculosis was introduced in March, 2006. The United States Center for Disease Control and Prevention (USCDC) plus world health organization has cooperatively published a report on tuberculosis [1]. However, lately extensively drug-resistant tuberculosis is cause main jeopardy to the worldwide switch of tuberculosis. Extensively drug-resistant tuberculosis is become increasingly prevalence in worldwide [2]. Extensively drug-resistant tuberculosis caused by bacterial strains resistant to isoniazid and rifampicin also referred as multidrug resistant, any of the fluoroquinolones, plus at least one of the three injectable second line drugs such as kanamycin, amikacin and capreomycin. Extensively drug-resistant tuberculosis (XDR-TB) is extremely burdensome to treat and is related with high mortality, especially in human immune deficiency virus infected patients. Extensively drug-resistant tuberculosis (XDR-TB) was reported in the 105 countries, and then roughly causes about 10% cases of multi-drug resistant tuberculosis.

Although extensively drug-resistant tuberculosis is being increasingly reported in especially non- rural areas in tuberculosis-endemically countries such as India, the absence of evaluate standards for drug susceptibility testing (DST) remains an utmost challenge in detection [3]. This review focuses on the extensively drug-resistant tuberculosis patients' prevalence, incidence, and disease burden in India.

Definition

The extensively drug-resistant tuberculosis defined as multidrug resistant tuberculosis and resistance to the fluoroquinolones plus at least one of the three injectable second line drugs i.e. amikacin, kanamycin and capreomycin [4]. Extensively drug resistant tuberculosis (XDR-TB) require resistance to the two most robust tuberculosis drugs such as isoniazid and rifampicin, in expansion to fight the any one of the fluoroquinolones such as levofloxacin or moxifloxacin, and at least one of three injectable second line drugs i.e. capreomycin, amikacin and kanamycin [4,5].

Approximately one in four population in global is affected with the tuberculosis bacteria. When the bacteria grow actively people become an inadequate upon tuberculosis. Bacteria develop active as a consequence of anything that can decrease the person's immunity, such as human immunodeficiency virus and some medical conditions [6]. Extensively drug resistant tuberculosis can develop when these second line drugs are also mismanaged and therefore also become inadequate. Extensively drug resistant tuberculosis increases concerns of a subsequently TB outbreak with confined medication choice, and threatens the major acquires made in tuberculosis resistor and the progress on decreasing tuberculosis bereavements between the people livelihood with (HIV/AIDS). It is consequently essential for the tuberculosis to manage properly, and new tools must be developed to prevention, treatment, and diagnosis of the disease [7].

Prevalence

The particular prevalence of extensively drug-resistant tuberculosis most regions in the world are presently unidentified. Though extensively drug-resistant tuberculosis was reported from India, extent and magnitude is yet to be determined. Efforts to expand observation of second-line tuberculosis drugs (SLDs) such as fluoroquinolone, aminoglycoside and ethionamide are in progress [8]. Due to constraints in resources and high tuberculosis burden, the resistance of fluoroquinolones and second line drugs is none tested routinely in the developing in the world. Exposure to fluoroquinolones and injectable aminoglycoside or both to treat bacterial infection other than tuberculosis may contribute to the evolution of resistance to these agents. India is the only country where tuberculosis is endemic and

fluoroquinolones and aminoglycosides are generally used, it is an important to know the prevalence of resistance to fluoroquinolones and aminoglycosides in mycobacterium tuberculosis isolates [9].

The national tuberculosis control programs working with all the health services can prevent extensively drug resistant tuberculosis by ensuring that all the specialist physicians working with tuberculosis patients adhere to the international standards for tuberculosis care.

According to the previous study reports on extensively drug resistant tuberculosis from India, it varied from 0.3 to 60% of multidrug-resistant tuberculosis as the sub-national community survey from India in 2006 in Gujarat reported extensively drug resistant tuberculosis 3.2% of 219 Multidrug-resistant tuberculosis patients [5]. All of the extensively drug resistant tuberculosis cases were previously treated cases. Another study shows the tuberculosis research center (TRC) and now the National Institute of Research on Tuberculosis (NIRT), Chennai, were reported 10 cases extensively drug resistant tuberculosis from cohorts study of 104 multidrug resistant tuberculosis cases. Among those extensively drug resistant tuberculosis patients, one was diagnosed pre-treatment; six had initial susceptibility to Kanamycin (Km) as well as Oflaxacin (Ofx), and three with only initial oflaxacin resistance [10].

Another study shows at a tertiary care tuberculosis hospital in New Delhi observed that 45 (20.17%) isolates were extensively drug resistant tuberculosis (XDR-TB) on analyzed sputum culture of 223 diagnosed multi-drug resistant tuberculosis (MDR-TB) patients. Most of the extensively drug resistant tuberculosis isolates showed resistance to the three or more drugs combination patterns, highlighting the need for urgent and timely sensitivity report for second line-drugs (SLDs) to help physicians start proper procedure to treat multidrug resistant tuberculosis patients to prevent with occurrence of extensively drug-resistant tuberculosis (XDR-TB). Previous studies show a tertiary care hospital at Delhi reported 24 (44.4%) isolates proven positive for Mycobacterium tuberculosis among 54 HIV-positive patients. Among the 24 isolates, 12 (50%) qualified for multidrug resistant tuberculosis, of which extensively drug-resistant tuberculosis (XDR-TB) resistance was observed (33.3%) of patients.

All the four extensively drug-resistant tuberculosis patients expired within 2.6 months of diagnosis. Another study on the drug resistance noticed in five Tibetan living in India reported that 14.5 per cent of 307 patients had multidrug resistant tuberculosis [10]. A cross sectional survey conducted among adults and children in the anti-retroviral therapy (ART)-center attendees in Mumbai revealed that drug resistance was diagnosed in 68 (34%) of the 202 culture-positive cases. A study conducted at four tertiary care hospitals in Delhi reported a prevalence of 3.7 % XDR-TB among 483 multidrug resistant tuberculosis patients [11].

According to the latest World health organizations (WHO) report, 8976 cases of multidrug resistant tuberculosis as well as Rifampicin Resistant tuberculosis (RR-TB) were trial for resistance to the second line-drugs with 3048 cases being extensively drug-resistant tuberculosis as confirmed by laboratory testing in India. Further studies are required at the community level from different regions of India to estimate the authentic incidence and prevalence rate of extensively drug-resistant tuberculosis to establish the early diagnosis of drug resistance and implementation of appropriate treatment strategy by the tuberculosis control program [12].

Incidence

The incidence of increasing multi drug-resistant tuberculosis and emergence of extensively drug resistant tuberculosis presents a tremendous challenge for global effort to battle with tuberculosis [13]. It is not feasible to measure incidence by counting cases arising in cohorts under continuous observation because such studies would require cohorts of hundreds of thousands of people. According to the previous studies of infection using tuberculin skin testing (TST) was used in the past to derive the estimates of incidence of tuberculosis, the interpretation of such surveys is often burdensome and their performance unpredictable [14].

XDR-TB is a rare type of the tuberculosis. However, almost 117 countries globally were reported at least one case of extensively drug-resistant tuberculosis every year. This information provided from the different countries with trustworthy data suggests that around 9.5% of multi-drug resistant tuberculosis (XDR-TB) instances of global have extensively drug-resistant tuberculosis. In 2015, there were estimated 485 000 incidence cases of multi-drug resistant tuberculosis in global among an estimated 590,000 incidence rifampicin-resistant tuberculosis instance [14]. Exclusively a small proportion of the extensively drug- resistant tuberculosis cases among all are detected, and numerous small and lower middle-income countries still lack adequate diagnostic capability to test for resistance to the second line drugs (SLDs) and thus observe extensively drug resistant tuberculosis [15].

Burden

India has a highest burden of tuberculosis in the world, accounting for 26% of the global incidence of tuberculosis. A considerably reinforced Revised National Tuberculosis Control Program is presently operating in India [15].

India is one of the countries with maximum burden of tuberculosis. As per world health organization tuberculosis figures from India for 2016 gives an estimated incidence about 2.79 million cases of tuberculosis from India [16]. Tuberculosis occurrence is the number of new instances of active tuberculosis disease during a certain time period.

India and china accounted almost 40% of the global tuberculosis cases. 3.6% of the new instances and 18-22% of earlier treated cases were estimated to have multidrug resistant tuberculosis India, China, The Russian Federation and South Africa has almost 55-65% of global cases of multidrug resistant tuberculosis. Worldwide, the emergence of drug resistance is a dangerous apprehension [17].

Recent published studies show that extensively drug resistant tuberculosis is related with high possibility of failure and death, and less chances of medications success than the multidrug resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) estimated around 40% of the Indian populations is infected with tuberculosis bacteria, the extensive majority of whom have a latent tuberculosis rather than tuberculosis disease. India apotheosis the lacunae of late diagnosis of drug resistance under the program conditions as many of the extensively drug resistant tuberculosis (XDR-TB) patients would have initially had multidrug resistant tuberculosis that slowly progressed to extensively drug resistant tuberculosis (XDR-TB) [18].

Treatment

The treatment of extensively drug-resistant tuberculosis is difficult and expensive. Less powerful agents are required for treatment because rifampicin and isoniazid cannot be used and drugs have to be used for a longer duration as well [19]. The treatment can be an individualized regimen or a standardized one, depending on the previous drugs taken by the patient (by constructing a drug-o-gram), degree of resistance in the community, and the financial status of the patient. A drug is examines to be effective of baseline drug susceptibility test (DST) shows susceptibility to that drug. However, if the drug susceptibility test results are not accessible, a drug may still consider being effective if not previously taken for at least one month. Another drug to be selected from group 2 is an injectable agent, to which the strain is susceptible, and its use can be extended to 12 months or more based on culture conversion [20].

It is recommended to use an injectable agent that has never been used so far or consider designing the regimen without an injectable agent in case of reported resistance to all injectable agents. If one of the injectable agents is considered effective but toxicity is a limiting factor, then an alternative route of inhalation through a nebulizer should be considered, but the use of this route is still questionable due to lack of evidence. Further, a drug from group 3 such as a higher generation fluoroquinolones (Moxifloxacin or Gatifloxacin) can be added. The use of all group 4 drugs that have not been used or less exposed in a previous regimen may be effective [21]. Two or more group 5 drugs [such as bedaquiline (Bdq)] can be added. Bedaquiline (TMC 207) is a recently approved drug by the world health organizations for the treatment of multi-drug resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB), which belongs to the diarylquinoline class of antibiotics. This drug has high bactericidal activity against drug resistance proved on the basis of a multicentric phase II trial. Delamanid (Dlm) and Pretomanid (Ptm) both are belong to the nitro imidazole class of antibiotics, currently undergoing phase II and phase III clinical trials [5].

Were 7250 extensively drug-resistant tuberculosis (XDR-TB) patients was enrolled on treatment in 58 countries and territories globally in the year of 2015. Most cases were from India (2130), South Africa (719), the Russian Federation (1205), and Ukraine (1206) [5]. The treatment outcomes of extensively drug-resistant tuberculosis (XDR-TB) vary widely depending on the drug regimens, duration of treatment, and the prevalence of tuberculosis and HIV, and even on geographical location. Usually, the outcome correlates with the spectrum of drug resistance. About 250,000 deaths were reported from multi drug resistant or rifampicin resistant tuberculosis in 2015 [22]. The latest data from cohort studies show a treatment success rate of 83%, 52%, and 28% for tuberculosis, multi drug resistant tuberculosis (MDR-TB) and extensively drug resistant tuberculosis (XDR-TB) respectively [23]. Previously, a detailed analysis of some observational studies found an overall 44% success rate for extensively drug-resistant tuberculosis (XDR-TB) treatment. In high burden countries, this rate may be even less [24]. In South Africa, less than 20% extensively drug-resistant tuberculosis patients became culture-negative after the treatment, and it was not dependent on the HIV status [25]. There are a few new drugs under development, and they have the potential to improve our capacity to treat extensively drug-resistant tuberculosis. For example, bedaquiline (diarylquinoline compound), and delamanid (nitro imidazole), have shown rapid culture conversion [26].

However, these drugs were not available before April 2015 to the National Tuberculosis Program (NTP) in most countries where extensively drug-resistant tuberculosis is most prevalent. As a result, by the end of 2015, bedaquiline and delamanid had been included in the drug regimens to treat multi-drug resistant tuberculosis (MDR-TB) were reported in 70 countries and extensively drug resistant tuberculosis were reported 39 countries respectively [26,27]. Very recently in 2016, the world health organization published treatment guidelines (updated version of the 2011 recommendation) for drug-resistant tuberculosis, primarily focusing on the composition of treatment regimes, effectiveness and safety of shorter regimes, and roles of surgery [28].

Conclusion

All the reference laboratories in each country should perform high quality conventional drug susceptibility test for all the second line drugs to diagnose extensively drug-resistant tuberculosis effectively. According to the previous study reports from across the India document the presence of extensively drug-resistant tuberculosis (XDR-TB) in India. There is a pressing need for country wise survey of extensively drug-resistant tuberculosis (XDR-TB). Huge enlargement of quality assured mycobacteriology laboratories should be providing a stern guidelines and etiquettes are essential for diagnosis and treatment of extensively drug-resistant tuberculosis. Practical and effective infection containment measures and facilities for intensive counselling of tuberculosis patients need to establish.

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