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Drug Resistant Tuberculosis — Is There Hope?

Manish Kumar Goel*, Pardeep Khanna**

* Assistant Professor,
** Senior Professor& Head
Department of Community Medicine, PGIMS, Rohtak, India

REVIEW

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Corresponding Author:
Manish Kumar Goel
Assistant professor,
Department of Community Medicine,
PGIMS, Rohtak, Haryana, India.
Email: drmanishgoel2000@yahoo.co.in

Abstract

Tuberculosis remains a worldwide public health problem. India has the highest burden of tuberculosis in the world and accounts for nearly 2/5th of global burden and 2/3rd of burden in SEAR countries. The XDR- TB was first described in March 2006 and has also been reported in India. The emergence of XDR – TB is associated with a very low probability cure and a high case fatality as evidenced by various researchers. Extensively drug-resistant tuberculosis is rapidly fatal if not treated. Some studies reveal a new and brighter perspective: even in developing countries, extensively drug-resistant tuberculosis may be cured in the majority of cases when management is aggressive and appropriate. What is required is action that is borne out of clear planning, financial commitment and adequate resources, technical capacity, and partnership. Increase in cure rates could be achieved by perfecting the supervision, support and monitoring concerning management of XDR-TB.

Key Words
Extensively drug-resistant tuberculosis; treatment; cure; developing countries

Tuberculosis remains a worldwide public health problem despite the fact that the causative agent was discovered more than a century ago and effective drugs and vaccine are available for its prevention and control.[1] India has the highest burden of tuberculosis in the world. It accounts for nearly 2/5th of global burden and 2/3rd of burden in South East Asia Region (SEAR). In spite of various effective treatment strategies adopted for control and prevention of tuberculosis throughout the world the mortality rates are still at a very high level.[2] In several countries where tuberculosis is rising rapidly, association with HIV along with the development of resistant strains is a serious concern.

Isoniazid and Rifampin are the anchors of standard first-line therapy.[3] Resistance to these two drugs, which defines multidrug-resistant tuberculosis, is associated with a decreased probability of cure.[4-6] Cure is defined as the patient who has completed treatment and has been consistently culture negative i.e. at least five consecutive negative results in the last 12 to 15 months. Patient can still be considered cured even if on one follow-up visits during the last three quarters the culture is positive, provided that this must be followed by at least three consecutive negative cultures taken at least 30 days apart.[7]

In India the prevalence of primary Multi Drug Resistant (MDR) tuberculosis is around 3% and MDR Tuberculosis in re-treatment cases is in the range of 12-17%.[8] Treatment regimens for multidrug-resistant tuberculosis rely on the most active second-line drug classes — fluoroquinolones and injectable agents (amikacin, capreomycin, and kanamycin)[9,10] For patients with infecting isolates that are resistant to three or more drugs in these classes now defined as extensively drug-resistant tuberculosis.[11]

This entity was first described in March 2006.[12] As of May 2009, more than 50 countries worldwide reported to the World Health Organization (WHO) at

least one case of extensively drug-resistant tuberculosis (XDR- TB).[13] The XDR- TB has been reported in India but the magnitude of the problem remains to be determined. The emergence of XDR – TB is associated with a very low probability cure and a high case fatality as evidenced by various researchers.[14-16]

A report from KwaZulu–Natal Province, Latvia, South Africa, suggested that in patients co-infected with human immunodeficiency virus (HIV), extensively drug-resistant tuberculosis is rapidly fatal if not treated.[17]

But evidence has also come from studies of mostly HIV-sero-negative patients in Europe, the United States, and Korea[14,15,18] where extensively drug-resistant tuberculosis was associated with much higher failure and mortality rates than multidrug-resistant tuberculosis. Some studies reveal a new and brighter perspective: even in developing and under developed countries, extensively drug-resistant tuberculosis may be cured in the majority of cases when management is aggressive and appropriate.[17, 19]

Essentials in the management of such patients are

1. Supervision- strict treatment supervision must be enforced. This is essential in managing extensive drug resistant cases of tuberculosis, particularly when second-line drugs are used. As with unsupervised treatment chances of creating additional drug resistance will exacerbate, and would result in worsening of an already catastrophic situation. However, supervision did not consist of merely monitoring people follow regimens; it must have all the elements of support for successful completion of designated treatment regimen.
2. Support- types of support needed are social and interactive support for minimizing the additional stress of patients because of prolonged hospitalizations. Psychological support is also needed for people taking potentially toxic drugs. Nutritional support along with financial incentives should also be provided to counteract the adverse effects of drugs and compensate for loss of wages respectively, so that adherence to treatment regimen remains un-interrupted.
3. Monitoring- Bacteriologic and clinical monitoring must be intense, allowing readjustments and optimization of the case-management approach.

They are all part of the Stop TB Strategy promoted by the WHO[20] and have been incorporated in recent international programmatic and care guidelines for drug-resistant cases.[21,22] If every national program put this strategy in place with equal vigor and assertiveness, drug resistance would be minimized and, when already present, effectively managed.

Only some studies, the Lima project[19] and the Latvia study[17], observed high rates of cure and low rates of fatality while rest of the studies elsewhere (even in the United States and Europe that specialize in the management of drug-resistant tuberculosis) [14,18] have not achieved such high rates. One possibility may be that the strains causing the disease in Peru were resistant to more drugs.

Individual care provided was very rigorous in metropolitan Lima and supervision of treatment and patient support provided was also of the same quality. In spite of all these, the unique aspect of the project was a strong partnership shared by a local non-governmental organization (NGO) that implemented care, A U.S. based NGO that provided technical expertise and financial resources, and the Ministry of Health of Peru that provided infrastructural and organizational support. Such partnership with established local capacity and a standard level of expertise is rarely found elsewhere.[23]

In 2008, it was observed that scaling up of services was the major challenge faced by most complex health interventions worldwide, especially when health systems and services are not optimal.[24] What is required is action that is borne out of clear planning, financial commitment and adequate resources, technical capacity, and partnership. Ultimately, the effectiveness of a complex intervention depends on coordinated work among all forces. The Peru experience is a clear example that, in this spirit, even the most difficult objectives can be reached. The challenge is to make this approach a sustainable reality worldwide. Increase in cure rates could be achieved by perfecting the use of current tools (like currently available drugs and technical and lab support) along with rapidly implementing new and effective strategies as and when evidence of success become available, such as quality - supervision, support and monitoring in case of management of XDR-TB.

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CONFLICTS OF INTEREST

The authors have no competing interests.