# The Threat of Multidrug-resistant Tuberculosis

Multidrug-resistant tuberculosis (MDR-TB) is one of the main challenges to TB control globally.[1] It has been defined as infection with *Mycobacterium tuberculosis* strains resistant to at least isoniazid and rifampicin.[1] The exact estimate of the incidence of this infection is difficult to obtain because of variations in testing and reporting in different regions of the world. World Health Organization (WHO) estimates state that approximately 480,000 new cases of MDR-TB occur each year all over the world. Out of them, almost 10% report additional drug resistance and are categorized as extensively drug-resistant TB. However, out of these estimated MDR-TB cases, only 132,000 cases were detected globally each year.[1] In other words, out of the estimated number of people with MDR-TB, only about 27% are actually detected, and an even lesser number are put on proper treatment each year. Hence, as the threat of MDR-TB is rising, there is still a wide chasm in case detection and treatment initiation rates. This is leading to increased morbidity and mortality due to TB. MDR-TB causes approximately 250,000 deaths globally each year, the majority of these being from Asia.[1]

India is the country with the highest burden of TB in the world.[2] Data released by the Ministry of Health in India state that approximately 3 million new cases of TB occur each year in the country.[2] The annual mean mortality from TB in India is 480,000.[2] Furthermore, according to 2010 WHO estimates, annual incidence of MDR-TB in India is approximately 99,000.[3] Surveys in selected parts of India have revealed that around 3% of new TB cases and 17% of relapse cases are MDR.[3] However, such figures may be an underestimate because proper diagnostic facilities and drug sensitivity testing are not available in many parts of the country. Furthermore, for extrapulmonary TB, the clinical specimens are not always suitable for drug sensitivity testing. Hence, while MDR-TB is easier to detect in pulmonary infections, it is often not diagnosed in extrapulmonary sites.

Treatment of MDR-TB is a difficult and prolonged undertaking. It requires multiple drugs, including injectable ones, for prolonged periods. Many of these have significant side effects which make treatment adherence difficult. Furthermore, the definition of "cure," as given by international bodies such as the WHO, has been criticized for inaccuracy.[4] Thus, with different regions using different definitions, it is very difficult to estimate the true impact of MDR-TB treatment. For example, one European study showed that while the WHO definition showed a cure rate of only 31% in MDR-TB, a simplified definition including relapse-free period increased that estimate to 61% in the same cohort of drug-resistant TB patients.[4]

In a study from South Africa, treatment success was documented in 48% of MDR-TB cases with a 20% death rate.[5] However, in another study from Switzerland, involving predominantly foreign nationals with MDR-TB, a 76% treatment success rate was documented.[6] However, in this Swiss patient cohort, the treatment regimens were variable with use of drugs such as linezolid and rifabutin.[6] In another study from South Korea, the trend in treatment success for MDR-TB was shown to improve significantly from 53% in 2000 to 83% in 2010.[7] This was said to be due to more frequent use of later generation fluoroquinolones and linezolid over the years. Thus, while assessing the data for treatment outcomes in MDR-TB, the actual treatment protocol used must also be known. Furthermore, since "cure" is often difficult to demonstrate objectively, "treatment success" is used as a surrogate marker in public health programs.

In the present issue of the journal, a study from North India on the treatment outcomes of MDR-TB has been published.[8] This was done in a public sector health facility following government protocols. This shows a cure rate of 52% and death rate of 16%. These patients were treated according to the Indian national TB control program, which follows the WHO recommendations.[9] The treatment outcome parameters were also defined according to the WHO guidelines. This treatment outcome data are similar to the South African study, while cure rates are much lower than studies reported from regions such as Switzerland and South Korea.

The treatment outcome statistics are not uniform in India. A study from a private sector hospital in India showed that 68% of MDR-TB cases were cured, while only 15% had treatment failure.[10] However, these patients were not treated according to the government protocol, and individualized drug regimens were given according to drug sensitivity testing.[10] This is possible in a state-of-the-art private facility with superior technical backup. However, most of the patients in low- and middle-income countries such as India are treated in public health facilities. Such advanced testing and individualization of drug regimen for each patient are always not feasible in the public sector.

MDR-TB continues to be a significant public health problem in many countries of the world, including India. Management of this resistant infection requires good diagnostic facilities. Furthermore, the patients often cannot tolerate the prolonged and painful treatment regimen. Such issues must be addressed in the program framework to combat this rising threat.

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