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Multi drug resistant tuberculosis: at the cross road in India

Khadanga S.[1*], Karuna T.[2], Behera S.[3], Dugar D.[4]

[1*] Sagar Khadanga, Associate Professor, Department of Medicine, LN Medical College, Bhopal, Madhya Pradesh, India.

[2] T Karuna, Assistant Professor, Department of Microbiology, AIIMS, Bhopal, Madhya Pradesh, India.

[3] Sarat Kumar Behera, Associate Professor, Department of TB and Chest, Hi tech Medical College, Bhubaneswar, Odisha, India.

[4] D Dugar, Assistant Professor, Department of Surgery, Hi tech Medical College, Bhubaneswar, Odisha, India.

Tuberculosis is endemic disease in India. Prevalence is very high and one third of our population is infected with this disease. Emergence of MDR form of Mycobacterium bacilli has further deteriorating Indian scenario. In this article we have discussed prevalence & preventive strategies for MDR form of Tuberculosis.

Keywords: MDR, Tuberculosis, Prevention, National Programme

Corresponding Author

Sagar Khadanga, Associate Professor, Department of Medicine, LN Medical College, Bhopal, Madhya Pradesh, India.
Email: sagarkhadanga@yahoo.com

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Introduction

In India, the first open air sanatorium for treatment and isolation of tuberculosis (TB) patients was founded in 1906 in Tiluania, near Ajmer city of Rajasthan, followed by the first TB dispensary in Bombay in 1917 and by 1925, chest radiology was available [1]. In 1951, India started the first nationwide mass BCG campaign to control TB in association with WHO [2]. In 1961, District Tuberculosis Program was prepared by the Indian government and Anantapur district in Andhra Pradesh was the first model district TB center (DTC) [2]. In 1992, Government of India, together with the WHO and the Swedish International Development Agency (SIDA), reviewed the National Tuberculosis Control Programme (NTCP) and concluded that it suffers from managerial weaknesses, inadequate funding, over-reliance on x-ray, nonstandard treatment regimens, low rates of treatment compliance and lack of systematic information on treatment outcomes [3]. In 1993, WHO declared TB to be a global emergency and devised the Directly Observed Treatment, Short course (DOTS) strategy. This strategy was built on five pillars;

- Political commitment and continued funding for TB control programs,
- Diagnosis by sputum smear examinations,
- Uninterrupted supply of high-quality anti-TB drugs,
- Drug intake under direct observation
- Accurate reporting and recording of all registered cases.

World Bank acknowledged that the DOTS strategy was the most economical health intervention and agreed to provide credit assistance for the NTCP. To give new thrust and to revitalize the NTCP, in 1997, the Revised National TB Control Program (RNTCP) was launched [4]. It formulated and adopted the internationally recommended DOTS strategy, as the most systematic and cost-effective approach to revitalize the TB control program in India. Today, India's DOTS program is the fastest-expanding and the largest program in the world in terms of patients initiated on treatment [5].

Since the early part of this century isolated cases of treatment failure cases among patients who completed DOTS were reported From India and the apprehension for drug resistance grew up. The emergence of resistance and particularly multidrug-resistant tuberculosis (MDR-TB) has become a significant public health problem in a number of countries including India. The available information from the several drug resistance surveillance studies conducted in several parts of country suggest that the rate of MDR-TB is relatively low in India [6]. However this translates into a large absolute number of cases. The first ever systematic survey in the year 2005, documented 0.04% of the TB cases in India were diagnosed and reported as MDR-TB which rose to 0.15% in the year 2007 [7]. The treatment success rate of 86% achieved in DOTS cohorts worldwide, exceeded the global target of 85% for the first time in 2007 [8]. But the reputation of DOTS was at stake on the emergence of resistant TB cases. Considering the serious implications of MDR tuberculosis in public health, WHO put forward the guidelines for the "Programmatic Management of Drug resistant Tuberculosis" (PMDT) in 2006. Since then it has revised the strategy in 2008 and 2011. After successfully establishing the DOTS service all over the country, RNTCP introduced the PMDT services in 2007 as DOTS plus. Government of India put forward the last PMDT guidelines in 2012 [6].

Drug Resistant Tuberculosis: Drug resistance may be broadly classified as primary and acquired. Drug resistance in a patient who has never received anti-TB treatment previously is termed as primary resistance. Acquired resistance is that which occurs as a result of specific previous treatment. WHO has now replaced the term primary resistance with the term *drug resistance among new cases*; and acquired resistance, with the term *drug resistance among previously treated cases* [9, 10]. Rifampicin resistance is most commonly encountered followed by Isoniazid. MDR-TB is defined as resistance to Isoniazid and Rifampicin, with or without resistance to other anti-TB drugs. Extensively drug-resistant TB (XDR-TB) is defined as resistance to at least Isoniazid and Rifampicin (i.e. MDR-TB) plus resistance to any of the fluoroquinolones and any one of the second-line injectable drugs (Amikacin, Kanamycin or Capreomycin) [6].

MDR-TB is a man-made phenomenon [6]. Poor treatment, poor drugs and poor adherence lead to the development of MDR-TB [6]. An inadequate or poorly administered treatment regimen allows drug-resistant mutants to become the dominant

Strain in a patient infected with TB. The common causes of drug resistance lies with the following 3 things [6];

- **Inadequate regimen** (inappropriate guidelines, non-compliance with guidelines, inadequate training of health staff, no monitoring of treatment, Poorly organized or funded TB control programme),
- **Inadequate supply or quality of drugs** (stockouts, poor storage conditions, wrong dosages or combination)
- **Inadequate drug intake** (poor adherence or poor DOT, non-availability of free drugs, adverse drug reactions, social and economic barriers, mal-absorption, substance abuse disorders).

According to the World Health Organization (WHO), of the world's 12 million people living with TB, an estimated 630,000 people had MDR-TB in 2011[11]. About 60% of these cases occur in Brazil, China, India, the Russian Federation and South Africa alone ("BRICS" countries) [11]. Prevalence of MDR-TB in India is about 3% in new cases and 12-17% in re-treatment cases [12]. Although the proportion is small, the number of persons with MDR-TB is sizeable in absolute numbers. WHO has estimated that in 2009, a total number of 99,000 cases of MDR TB emerged in this country including those outside RNTCP [6]. Among these, 64,000 were estimated to have emerged from TB cases notified to RNTCP [6]. If left undiagnosed or poorly treated, MDR-TB patients transmit the disease in the community before they die.

Approximately 9% of MDR-TB cases are extensively drug-resistant TB (XDR-TB) [13]. As of October 2012, 84 countries had reported at least one XDR-TB case including India [13]. It is impossible to tackle theproblem of drug-resistant TB through treatment alone; each MDRTB case costs more than 20 times the cost of a simple drug-susceptible TB case. Prevention of emergence of MDR-TB in the community is more imperative rather than its treatment [6]. The treatment requires many short acting, less effective, costly and sometimes toxic drugs to be given for nearly 2 years in a tertiary care health centre in isolation [13]. The association of MDR-TB with AIDS creates havoc both to the society and to the managerial staff. "Programmatic Management of Drug resistant Tuberculosis" (PMDT) remain as the single most and effective method to combat MDR and XDR tuberculosis [6]. PMDT

Is more complex than the basic DOTS strategy. For PMDT to be successful, special attention is needed for the following [6]:

- Efficient and timely identification of patients who require drug sensitivity testing(DST);
- Quality-assured laboratory capacity (Smear, Culture-DST, rapid molecular test);
- Efficient drug procurement and supply chain management;
- Adherence to difficult-to-take regimens for long periods;
- Prompt identification and management of sideeffects;
- Recording and reporting; and
- Human and financial resources.

Conclusion

In order to intensify our fight against this deadly disease, we need to further strengthen our surveillance programs to accurately estimate the burden of all kinds of TB (childhood, pregnancy, HIV/TB, MDR-TB). There is a dire need to regulate the rational use of first and second line anti-TB drugs. They should absolutely not to be sold as *over the counter* (OTC) drugs [6]. All cases and all treating physicians (government or private sector) treating the TB cases should be notified [6]. Among all these fearful facts of MDR-TB, still remain a silver lining ray of hope as in 2011, about 18% of cases of MDR-TB were placed on treatment and the 75% treatment success target was achieved by 30 countries [13]. WHO with its "**STOP TB**" strategy has given a vision to eliminate TB as a public health problem from the face of this earth by 2050 [7]. We have come a long way in our fight against this deadly disease, but as the famous English poet Robert Frost said, "… miles to go before I sleep", we still have much more to accomplish to make the world TB free.

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