

## New short-course regimen in multidrug-resistant tuberculosis control- A need of the hour

Sankalp Yadav<sup>1,\*</sup>, Gautam Rawal<sup>2</sup>, Mohammad Atif<sup>3</sup>

<sup>1,3</sup>General Duty Medical Officer II, <sup>2</sup>Associate Consultant, <sup>1,3</sup>Dept. of Medicine & TB, Chest Clinic, Moti Nagar, North Delhi Municipal Corporation, New Delhi, <sup>2</sup>Respiratory Intensive Care, Max Super Specialty Hospital, New Delhi, India

**\*Corresponding Author:**

Email: drsankalpyadav@gmail.com

Drug resistant TB (DR-TB) has threatened the global TB control efforts [1]. A growing number of such cases could be attributed to the ever increasing population and to the increased awareness about the disease, due to a large scale IEC activities and advertisements in the media [2].

The routine treatment of DR-TB like multidrug-resistant TB (MDR-TB) is associated with a high pill burden, multiple adverse drug reactions (ADR's) and longer treatment duration [3-5]. This has led to a number of lost to follow-up cases, treatment failures, deaths and even development of extensively drug resistant (XDR-TB) cases [5].

To overcome this problem on May 2016, a new regimen shorter in duration of 9-12 months is endorsed by the WHO based on the meta-analysis studies done by the Union, Damien Foundation, Medecins Sans Frontieres and the Antwerp Institute of Tropical Medicine in Belgium, involving a large number of patients with uncomplicated MDR-TB [6-9].

This short-course regimen also famous as 'Bangladesh regimen' being started post initial studies in Bangladesh is intended for the Rifampicin resistance (RR-TB) and MDR-TB cases who have not been previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents has been excluded or is considered highly unlikely [10]. WHO recommends a detailed work-up for detecting resistance to fluoroquinolones and injectable second-line anti-TB drugs [11].

The short-course MDR regimen involves an intensive phase of four months (extended to six months in case of delayed sputum smear conversion) containing high-dose Gatifloxacin or Moxifloxacin, Kanamycin, Prothionamide, Clofazimine, high-dose Isoniazid, Pyrazinamide and Ethambutol followed by a continuation phase of five months containing Clofazimine, Gatifloxacin or Moxifloxacin, Pyrazinamide and Ethambutol and can be started in uncomplicated MDR-TB children, adults and people living with HIV who meet the inclusion criteria [12]. However, this regimen is not recommended for extrapulmonary TB cases and in pregnant women [12].

The benefits of this regimen are a lot as the short duration leads to greater compliance and adherence of the patients to the treatment, thereby reducing the number of lost to follow-up cases [12]. It also has a

remarkable impact on the number of toxic effects of drugs, as the total duration of treatment is almost halved and the ADR's have always been a major contributor to the treatment failure or lost to follow-up cases [13]. Also, it is a much cheaper regimen and costs less than USD1000 per patient [13]. The published literature shows that the treatment success rate of this shorter regimen is 89.9% as compared to 78.3% in the conventional regimen [12].

Besides, this regimen will also reduce the burden on the already overburdened health staff working in the DR-TB care [12]. The shorter treatment duration will be a boon to the already grave situation in the high TB burden countries like India [12]. And one of the very important aspects of this regimen is that it can be given in HIV prevalent settings as well [14]. The resources freed by the short-course regimen may be utilized to increase the reach and accessibility of the TB control program, thus having an impact on the health budget of the high TB burden countries [12].

However, there are certain snags associated with this newer short-course regimen [13]. There is a need of rapid DST and in many settings such fast results of DST may not be available and this could hamper the initiation of this regimen [13]. Also, this may lead to higher chances of decreased effectiveness and diminished short-term benefit, as well as long-term risk of amplified second-line drug resistance [13]. The regimen relies on a number of drugs to which baseline resistance has been reported in certain populations [15,16]. There is a baseline resistance to fluoroquinolones or second-generation aminoglycosides to the extent of 10%, thus depriving these groups from this highly beneficial regimen [13]. The reliance on Pyrazinamide in the new regimen with an evidence of a baseline resistance to the extent of 35-81% in MDR strains needs to be taken care of especially in high burden settings as the majority of such cases will be excluded from the new short-course regimen [15,17].

Thus, a shorter, cheaper, more effective, and more tolerable new regimen is the need of the hour and might prove to be a solution to the ever growing MDR-TB cases. The new regimen may reduce the TB incidence by 20%, however, before coming to such major conclusions, evidence from multiple randomized controlled trials with a sizeable data from endemic countries is imperative. Furthermore, in the fight

against TB this short-course regimen is a big ray of hope and may prove to be helpful in reducing the mortality and morbidity associated with the disease.

**Conflicts of Interest:** None declared

**Acknowledgements:** None

## References

1. Moodley R, Godec TR, STREAM Trial Team. Short-course treatment for multidrug-resistant tuberculosis: the STREAM trials. *Eur Respir Rev.* 2016;25(139):29-35.
2. Yadav S. A new concept in tuberculosis awareness in the low income countries. *Edorium J Tuberc.* 2015;5:1-4.
3. Geneva: WHO; 2014. World Health Organization. Companion handbook to the WHO guidelines for the programmatic management of drug resistant tuberculosis. WHO/HTM/TB/2014.11.
4. Central TB Division. Guidelines on Programmatic Management of drug Resistant TB (PMDT) in India. New Delhi: Directorate of General Health Services, Ministry of Health and Family Welfare, Government of India; 2012.
5. Vasisht AK, Yadav S. Role of a counselor in the management of multidrug-resistant TB. *Indian Journal of Immunology and Respiratory Medicine.* 2016;1(1):23-4.
6. Geneva: WHO; 2016. World Health Organization. WHO Treatment Guidelines for Drug-Resistant Tuberculosis 2016 Update. WHO/HTM/TB/2016.04.
7. Van Deun A, Maug AKJ, Salim MAH, Das PK, Sarker MR, Daru P, et al. Short, highly effective, and inexpensive standardized treatment of multidrug-resistant tuberculosis. *Am J Respir Crit Care Med.* 2010;182:684-92.
8. Kuaban C, Noeske J, Rieder HL, Ait-Khaled N, Abena Foe JL, Trébucq A, et al. High effectiveness of a 12-month regimen for MDR-TB patients in cameroon. *Int J Tuberc Lung Dis.* 2015;19:517-24.
9. Piubello A, Harouna SH, Souleymane MB, Boukary I, Morou S, Daouda M, et al. High cure rate with standardised short-course multidrug-resistant tuberculosis treatment in Niger: No relapses. *Int J Tuberc Lung Dis.* 2014;18:1188-94.
10. Aung KJM, Van Deun A, Declercq E. Successful '9-month Bangladesh regimen' for multidrug-resistant tuberculosis among over 500 consecutive patients. *Int J Tuberc Lung Dis.* 2014;18:1180-187.
11. Geneva: WHO; 2016. World Health Organization. The Use of Molecular Line Probe Assays for the Detection of Resistance to Second-Line Anti-Tuberculosis Drugs. WHO/HTM/TB/2016.07.
12. Prasad R, Gupta N, Banka A. Shorter & cheaper regimen to treat multidrug-resistant tuberculosis: A new hope. *Indian J Med Res.* 2017;146(3):301-03.
13. Kendall EA, Fojo AT, Dowdy DW. Expected effects of adopting a 9 month regimen for multidrug-resistant tuberculosis: a population modelling analysis. *Lancet Respir Med.* 2017;5(3):191-99.
14. Trébucq A, Schwoebel V, Kuaban C, Kashongwe Munogolo Z, Fikouma V, Bakayoko A, et al. Expanding shortened MDR-TB treatment: The West African experience. *Int J Tuberc Lung Dis.* 2014;18(Suppl 1):S15.
15. Zignol M, Dean AS, Alikhanova N. Population-based resistance of Mycobacterium tuberculosis isolates to pyrazinamide and fluoroquinolones: results from a multicountry surveillance project. *Lancet Infect Dis.* 2016;16:1185-192.
16. Cegielski JP, Kurbatova E, van der Walt M. Multidrug-resistant tuberculosis treatment outcomes in relation to treatment and initial versus acquired second-line drug resistance. *Clin Infect Dis.* 2016;62:418-30.
17. Skrahina A, Hurevich H, Zalutskaya A. Alarming levels of drug-resistant tuberculosis in Belarus: results of a survey in Minsk. *Eur Respir J.* 2012;39:1425-431.