

The current updates in the TB control program of India

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The last five years have seen a revolutionary change in the management of the oldest infectious disease known to mankind [1]. The aggressive approach to find and cure the missed cases over and above treating the regular patient load has contributed greatly towards the efforts aimed at TB elimination by 2025 [1]. Besides, a number of active interventions have also provided valuable data which will help in determining the overall prevalence of the disease in society [1]. The major contributors for this success involve the government's schemes like daily DOTS, active case finding, Nikshay Poshan Yojna, direct benefit transfer (DBT), universal DST, Joint Efforts to Eliminate TB (JEET), etc. [1-3]. These along with other remarkable developments like the availability of free of cost investigations (CBNAAT, LPA, culture, etc.) and also the free access to newer drugs like Bedaquiline (BDQ) and Delamanid have contributed significantly in the fight against TB [1]. The whole national program i.e., Revised National Tuberculosis Control Program (RNTCP) has got a boost with increased surveillance and monitoring [1]. The present paper highlights the latest developments in India's TB control program.

Change of Weight Band

TB patients up to eighteen years of age should be given treatment as per the chart of child dosages as children in both drug sensitive and resistant cases [4,5].

As recommended by WHO for ensuring the optimal dosage in adult TB cases the weight categories for the use of fixed-dose combination's (FDC's) in adults are revised for the first line antitubercular drugs [4] (Table 1).

Table 1: Weight categories for the use of FDC's in adults

Weight category (KG)	Number of tablets (FDC's)	
	Intensive Phase-4FDC (HRZE) 75/150/400/275	Continuation Phase-3FDC (HRE) 75/150/275
25-34	2	2
35-49	3	3
50-64	4	4
65-75	5	5
>75*	6	6

*Patient more than 75kg may receive 5 tablets/day if they do not tolerate the revised dose

In cases with a five kilogram or more increase or decrease in weight from the baseline, the weight category

with appropriate FDC should be changed as per the RNTCP guidelines [6].

Change in Isoniazid (H)-mono/poly Resistance Regimen

The management of H-Mono resistance involved the use of injectable i.e., Kanamycin (Km) [1]. And the duration of the treatment was nine to twelve months with an initiation phase (IP) of (3-6) months and a continuation phase of six months [1]. The latest changes in this regimen involve the complete omission of injection Km in both the pulmonary and extrapulmonary cases [1]. Also, the total duration of the regimen will be six months with no separate intensive phase (IP) or continuation phase (CP). The new regimen will involve all the old drugs Levofloxacin, Rifampicin, and Pyrazinamide except the injectable Km [1]. The new regimen will be used in all prospective cases and the cases which were put on treatment before this change will continue to receive the old regimen [1]. The weight bands to be followed will be as per the Programmatic Management of Drug Resistant TB (PMDT)-2017 guidelines [7].

All the new cases will be started at the district/Nodal DR-TB center post confirmation of the H-mono/poly resistance [1,7]. A baseline SL-LPA for finding the additional resistance to fluoroquinolones is mandatory in all such cases [1]. However, the results of the same should not be the awaited and the standard six-month H-mono/poly regimen should be started [1]. The same regimen can be modified as per the PMDT guidelines in case of any other resistance on SL-LPA or on extended DST [7].

There is also a change in the pre-treatment evaluation with the omission of audiometry, serum creatinine and serum urea [7]. The follow-up involves smear microscopy every month after completion of first three months till completion of treatment [7]. Culture should be done in the third month, end of treatment and post-treatment follow-up at the end of 6, 12, 18 and 24 months [7]. In case the smear or culture comes out to be positive the patient should be offered CBNAAT or SL-LPA to determine any additional resistance to any other drug for which an appropriate regimen change as per the RNTCP-PMDT guidelines will be done [7]. All those cases with an extensive lesion; uncontrolled comorbidity; culture positive at the end of the third month or in extrapulmonary cases, the treatment can be extended to a month (up to a maximum of nine months) [7]. And for exceptional cases like military TB treatment may be continued for a year [7]. Treatment outcome definitions of cure; treatment completed; died; lost to follow-up; not evaluated and regimen change will be same as per the PMDT

guidelines [7]. Cases who remain smear positive after five months of treatment or beyond will be declared as treatment failure [7].

The Evaluation of a Standardised Treatment Regimen of Anti-tuberculosis Drugs for Patients with Multidrug-resistant Tuberculosis (STREAM) 2 trials

The successful adoption and implementation of the newer short course regimen for MDR-TB cases was a result of the STREAM 1 trials, wherein the new regimen was found to be as effective as that of the longer regimen of 22-24 months [8]. However, this short course regimen is associated with a lot of toxic drugs including the injectable [9]. To overcome this problem the STREAM 2 trial has started in which the efforts will be aimed to replace injection Km with BDQ or using a combination of Km and BDQ to replace Ethionamide (Eto) and Ethambutol (E) [10]. The main aim of this trial is to determine if the regimen can further be reduced. It is the first international multicentric randomized control trial where BDQ is used in the management of MDR-TB cases [10]. Presently this trial is carried in few selected countries and in India, it is conducted at three sites namely, RBIPMT-Delhi, NIRT-Chennai, and BJMC-Ahmedabad.

The STREAM-2 trial will have three arms i.e., a control arm- with current drugs of shorter regimen; the next arm will have injection Km being replaced by BDQ for the same duration of 40 weeks; and a third arm where Km and BDQ combination will replace ETO and E with an IP of two months and duration of 28 weeks [10]. The unique part of this trial involves the extensive pharmacokinetic studies for serum drug levels in the study subjects which will be the first time done in any trial in India in MDR-TB cases.

All adult, pulmonary, non-pregnant, smear-positive MDR-TB cases will be counseled and after obtaining a written informed consent in their language, will be admitted for a minimum 14 days post pretreatment evaluation and will be randomly assigned in any of the three arms of the trial. The most important part of this trial is the post-randomization follow-up of study subjects until 132 weeks [10]. Appropriate incentive better than the standard DBT will be provided to the patients and the treatment supporters.

To conclude, the government of India has made remarkable developments to achieve the national target of TB elimination by 2025. All the stakeholders have been involved and efforts aimed at achieving the same have become the need of the hour. Besides, these active interventions have contributed significantly in early diagnosis and management of the deadly infectious disease.

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