Do we Need to be More Updated in Pediatric Tuberculosis?

We read with interest the recent review article by Khurana, *et al*. [1], published in *Indian Pediatrics*. Pediatric tuberculosis (TB) used to be a neglected topic; however, it is heartening that national and international bodies are now taking interest in it and providing practical guidelines and their updates. In this article, the authors had presented a review of new developments in pediatric TB, which may prove to be very helpful for the general pediatricians. However, the recently updated guidelines developed jointly by Revised National Tuberculosis Control Programme (RNTCP) and Indian Academy of Pediatrics (IAP), and WHO Consolidated Guidelines on drug-resistant TB 2019 have provided some more changes that have not been incorporated in this review article [2,3].

1. There is a substantial change in the new case definition of presumptive pediatric TB; it refers to children with persistent fever and/or cough for more than two weeks with loss of weight / no weight gain and/ or history of contact with infectious TB cases. In this article [1], cough was given more importance; however, fever is a more significant symptom of pediatric TB. Furthermore, authors did not mention about history of contact with infectious TB cases, which is an important supportive feature in the diagnosis of pediatric TB [3].
2. In newly updated guidelines, chest *X*-ray and tuberculin skin test are advised to be performed upfront in cases of presumptive pediatric TB, which is considered as a significant change from the earlier guidelines. If *X*-ray is highly suggestive of TB (miliary, hilar or mediastinal lymphadenopathy, fibro-cavitory lesion) or shows persistent non-specific shadow even after a course of antibiotics, only microbiological sample is recommended [2,3]. However, this review article suggests that both smear examination and chest *X*-ray should be done upfront.
3. In previous guidelines and as per this review [1], Cartridge based nucleic acid assay (CBNAAT) is to be performed on the second sample if the first smear is negative, while as per the newly updated guidelines, CBNAAT is considered as the investigation of choice, and it should be ordered upfront in the first sample. Furthermore, in new guidelines, the preferred term is WHO-approved Rapid Diagnostic Test (WRDT), which also include Line probe assay (LPA) and Loop-mediated isothermal amplification (LAMP) apart from CBNAAT [2,3].
4. Category II anti-tubercular therapy (ATT) which was used to treat previously treated cases of TB has been withdrawn from newly updated guideline as it may lead to increased incidence of drug-resistant TB (DRTB) at the cost of low success rate [2]. In such cases, both WHO and RNTCP guideline now recommend that treatment should be guided by drug susceptibility test.
5. In contrast to what authors have mentioned, there are also significant changes in the treatment of DRTB. Now, the second line of drugs has been reclassified. As per new guidelines, Bedaquiline may be used in children 6-17 years of age with MDR TB. Delamanid may be included in the longer regimen for the treatment of MDR/RR-TB patients aged ≥3 years [4]. Furthermore, for the treatment of isolated isoniazid (INH) resistance, the new guidelines recommend replacement of INH with levofloxacin only [2].
6. In this article, there is no mention about pyridoxine supplementation, which is recommended in all pediatric TB cases as INH is now being used in a higher dose (10-15 mg/kg/day), and high prevalence of coexisting malnutrition increases the risk of INH toxicity. Furthermore, latent TB gets priority in the updated guideline, and INH prophylaxis is now recommended even in children ≥5 years of age with a positive skin test and history of TB contact, after exclusion of active TB [5].

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Updated Pediatric Tuberculosis Guidelines

We read with interest the review article by Khurana, *et al.* [1], published recently in *Indian Pediatrics.* We would like to highlight the recent changes in the management of pediatric tuberculosis (TB) based on Revised National Tuberculosis Control Programme (RNTCP) Updated Pediatric TB Guidelines 2019 and WHO consolidated guidelines on drug resistant tuberculosis treatment 2019 [2].

Changes in diagnostic algorithm: As tuberculosis is a paucibacillary disease in children, performance of smear microscopy and culture is poor. Hence, Cartridge based nucleic acid assay (CBNAAT) is the preferred investigation of choice over smear examination (and best yield when ordered based on positive chest *X*-ray). If CBNAAT is not available, smear microscopy is to be performed.

Newer classification of drugs: The drugs for multidrug resistant tuberculosis (MDR-TB) have been recategrized into three groups. Thus, Box 2 of the review article needs revision.

Changes in treatment approach for previously treated cases: Previously treated TB includes (recurrence, treatment after loss to follow-up and treatment failure). All these children need to be evaluated for drug-resistant TB. In case they are found to be drug sensitive, they shall be started on the same regimen as for a newly diagnosed case. Category II has been now withdrawn from RNTCP. Streptomycin is now considered as second-line medicine, and should be used only as a substitute for Amikacin, when it is not available or confirmed resistance to it.

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AUTHORS' REPLY

We agree with the readers about the issues that have been mentioned. As our manuscript was drafted and submitted for publication much before the new revised RNTCP–IAP guidelines were released, these changes could not be incorporated in the review article. Further, we would like to add a few more updates:

1. Presumptive drug-resistant tuberculosis (DRTB) is diagnosed in a patient who needs to be subjected to genotypic (CBNAAT, LPA) or phenotypic (LC-DST) drug sensitivity tests (DSTs) while probable MDR-TB is diagnosed in a patient, who after getting the results of the above tests, cannot be microbiologically confirmed and needs to be started on DRTB regimen based on their clinical and /or radiological deterioration (clinically diagnosed case of MDR TB).

2. Drugs used for second-line Anti-tubercular therapy (ATT) have been re-categorized as group A (Levofloxacin/Moxifloxacin, Bedaquiline and Linezolid), group B (Clofazimine and Cycloserine/ Terazodone) and group C (Ethambutol, Delamanid, Pyrazinamide, Amikacin/Streptomycin, Para-amino salicylic acid, Imipenem Cilastin/Meropenem and Ethionamide/Prothionamide). This re-grouping is more relevant to design longer duration standard MDR-TB regimens. Group A drugs are most relevant to design longer duration MDR-TB regimens followed by group B; group C drugs are used only if other cannot be used for some reason [1]. The shorter MDR regimen of 9-12 months with seven second-line ATT drugs has gained acceptance by the WHO as well as RNTCP. The 4-6 months intensive phase consists of Moxifloxacin, Ethambutol, Clofazimine, Pyrazinamide, Kanamycin, high-dose Isoniazid, and Ethiomanide. The continuation phase of 5 months consists of former four drugs only. This shorter regimen has been included for pulmonary pediatric MDR-TB patients or those with isolated lymph nodes or pleural effusion.

3. Delamanid may be included in the treatment of MDR/ RR-TB patients aged 3 years or more on longer