

Tuberculosis (TB), a disease mainly caused by *Mycobacterium tuberculosis*, is most commonly transmitted by inhalation of the infected droplets released by a patient with TB having cough and sneezing. TB mainly affects the lungs (pulmonary TB) but can involve any other organs like lymph nodes, pleura, bones and joints, genitourinary tract, nervous system, abdomen, skin (extra-pulmonary TB). Pulmonary TB is infectious.

EPIDEMIOLOGY

Along with HIV, TB now is a leading cause of death worldwide and in India it kills more adults than any other infectious disease (Figure 1). India with one sixth of global population has nearly a quarter (23%) of the global burden of tuberculosis i.e 2.2 million out of 9.6 million patients annually. Out of these about 2.2 lakh cases die annually. About 40% of the population is infected with this organism (prevalence of diseases). The lifetime risk of breaking down to disease in non HIV patients is about 10-15% as compared to HIV persons where it is 10% per year. More than 6000 persons develop TB and more than 600 die of this disease every day. Based on the Global TB report of 2015, India has the highest burden of both TB and MDRTB and second highest burden of HIV & TB.

CLINICAL FEATURES

Early case detection and diagnosis is vital to break the transmission of this disease. The patients having clinical symptoms i.e cough >2 weeks, fever >2 weeks, haemoptysis, significant weight loss and any abnormality in chest x-ray should be suspected to have tuberculosis and is called presumptive Pulmonary TB patients.

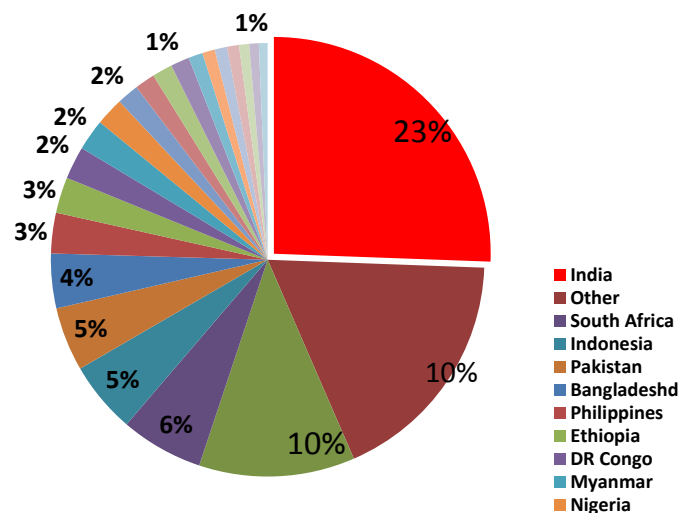


Fig. 1: Countries with High TB Burden

Patients on steroids or immunosuppression, contacts of pulmonary TB, patients living with HIV and AIDS (PLHIV), malnourishment and cancer should be screened for TB.

Presumptive extra-pulmonary TB (EPTB) is suspected in patients with any organs specific symptoms e.g swelling of a node, or any constitutional symptoms as fever >2 weeks, night sweats and weight loss.

Presumptive drug resistant TB (DRTB) is suspected in patients who have failed on first line medicines, contacts of DRTB patients and any follow up sputum positive TB patients.

The clinician should be well aware of the suggestive radiographic findings, awareness of co-morbidities and awareness of epidemiological circumstances that can increase the risk of TB.

DIAGNOSIS

The following methods are being used for the diagnosis of TB under RNTCP:

SPUTUM MICROSCOPY

The oldest method though with less sensitivity is being commonly used for the diagnosis of pulmonary TB. Both the ZN staining based microscopy and light emission diode based fluorescent microscopy (LED FM) is being used under the RNTCP and is available at all the nearest government laboratories.

CULTURE

Various culture based methods are being used under RNTCP but these methods take 6-8 weeks thus cannot be used for early diagnosis of TB. Under RNTCP these are recommended for the follow up of the DR TB patients.

Rapid Molecular Based Line probe assay (LPA) and Nucleic acid amplification test (NAAT) are being used for the detection of resistance of rifampicin and Isoniazid in the patients suspected to have DR TB. These methods are being used for both the sputum specimens and the specimens from extra-pulmonary sites. All patients groups with PLHIV, paediatric population, EPTB should be referred for CBNAAT in the beginning.

RADIOLOGY

Xray is to be used as a screening tool and any abnormality in chest radiograph should be confirmed by any of the above mentioned tests. Careful clinical history should be taken to support the diagnosis on Xray.

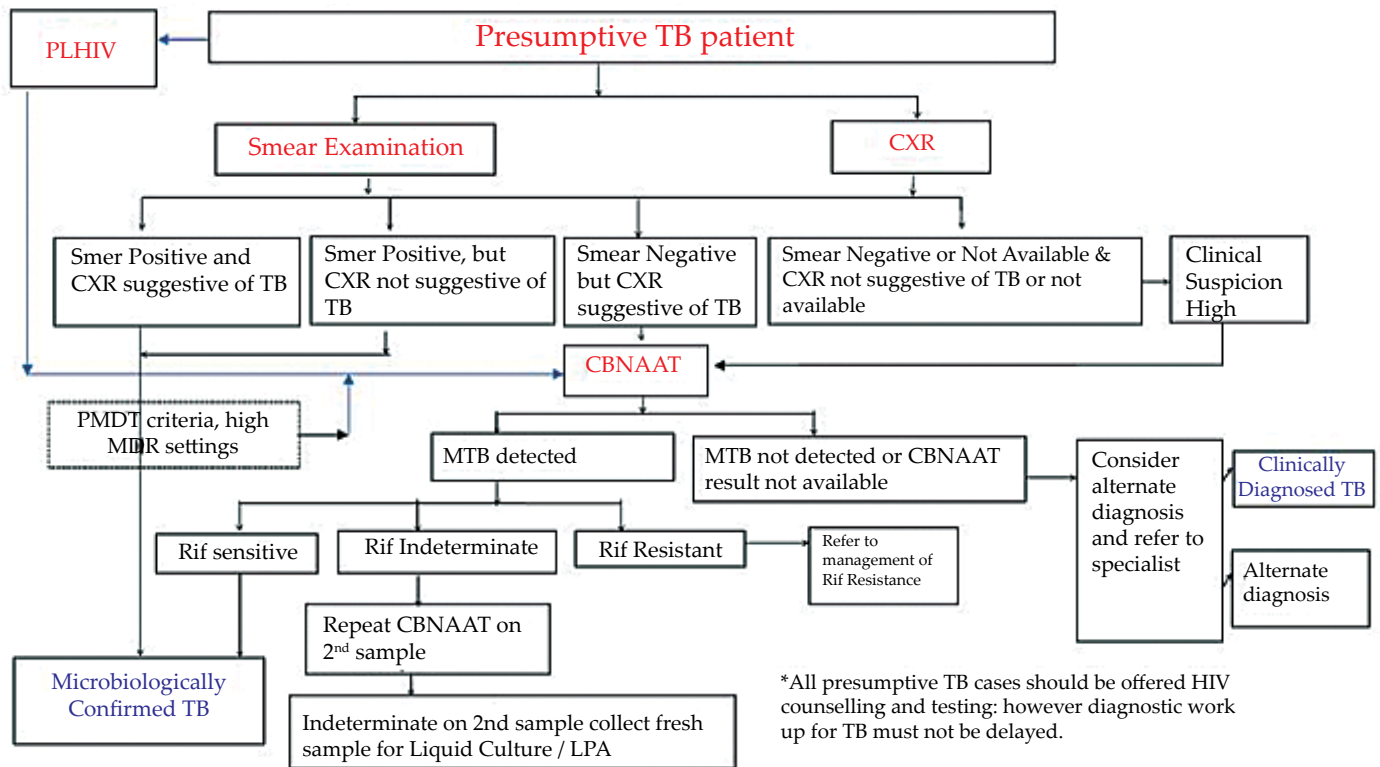


Fig. 2: Diagnostic Algorithm for Pulmonary TB

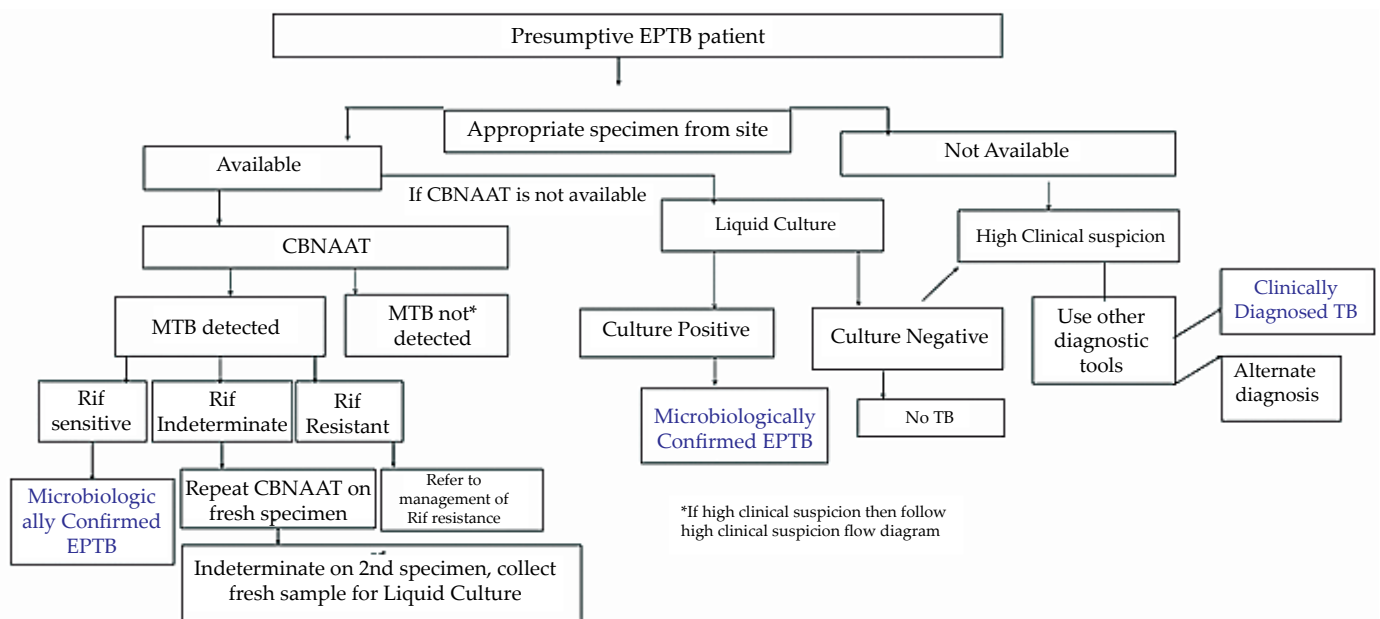


Fig. 3: Diagnostic Algorithm for Extra Pulmonary TB

TUBERCULIN SKIN TEST (TST) & INTERFERON GAMMA RELEASE ASSAY (IGRA)

TST or Mantoux test is to be used as an additional test after the absence of microbiological confirmation and a high clinical and radiological suspicion. Role of IGRA or TB Gold test in a high prevalence country like India is not clear hence not recommended.

SEROLOGICAL TEST

These tests are not recommended for diagnosis of TB and have been banned by the government.

DIAGNOSIS OF PULMONARY TB

All patients of presumptive TB should undergo various diagnostic tests to confirm the diagnosis as per the algorithm (Figure 2).

DIAGNOSIS OF EXTRA-PULMONARY TB (FIGURE 3)

A high level of suspicion is required to suspect EPTB in patients with signs and symptoms suggestive of the disease. Microbiological confirmation should be tried in all the patients suspected of EPTB. Specimens from the suspected sites should be obtained for smear microscopy, culture, CBNAAT or histopathology. Liquid culture is the

Table 1: Treatment based on Type of Case

Type of TB case	Treatment regime in Intensive phase (IP)	Treatment regime in Continuous phase (CP)
New	(2) Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E)	(4) Isoniazid (H), Rifampicin (R), Ethambutol (E)
Previously treated	(2) HRZES + (1) HRZE	(5) HRE

Table 2: Medicines and Weight of Patients

Weight category	Number of tablets (FDCs)		Inj. Streptomycin gm
	Intensive Phase HRZE 75 / 150 / 400 / 275	Continuation phase HRE 75 / 150 / 275	
25-39 kg	2	2	0.5
40-54 kg	3	3	0.75
55-69 kg	4	4	1
≥ 70	5	5	1

gold standard for diagnosis but it takes 2-8 weeks for the diagnosis. CBNAAT is preferred choice over other tests. Radiological investigations can be used as supporting tools for the suspicion and diagnosis of EPTB.

It is important to know the role of CBNAAT for EPTB diagnosis. Sensitivity of this test is high for FNAC/biopsy specimens from lymph nodes, other tissues and CSF but is lower for pericardial, ascitic and synovial fluid samples and further lower for pleural fluid. Positive test is useful but a negative test does not rule out TB. Tissues for CBNAAT should be collected without formalin.

TREATMENT

The goals of treatment of TB is to decrease the mortality and morbidity, prevent the development of drug resistance and to break the chain of transmission at the earliest by making the patient non-infectious and hence decrease the number of infectious patients.

The patients are classified as:

1. New case- A diagnosed TB patients who has never taken treatment for TB or has taken anti-TB medicines for less than one month.
2. Previously treated patients are the ones who have previously taken treatment for more than one month.
 - a. Recurrent TB cases are the patients who were previously declared cured or treatment completed and has now been microbiologically confirmed as TB.
 - b. Treatment after failure is the patients who have failed on treatment at the end of their course.
3. Treatment after lost to follow up- a patients who has been treated for TB for one month or more but did not continue the treatment and has now been microbiologically confirmed to have TB.

4. Other previously treated patients are the ones who have been treated for TB but the outcome is not known.

All TB patients should be offered HIV counselling and testing and should also be tested for diabetes.

The type of treatment depends on the classification of the cases and is shown in the Table 1 below.

The duration of CP may be extended by three to six months in situations like bone and joint involvement, spinal TB with neurological involvement and neuro-tuberculosis.

It is recommended to give daily regime under direct supervision. Fixed dose combinations of the drugs are recommended. The medicines are given as per the weight bands (Table 2). The medicines in FDCs will be available in Pilot districts and then introduced all over India. At present the medicines are available separately in blister packs.

MONITORING

Monitoring of the patients is very important for the success of the treatment. In patients with pulmonary TB (new and retreatment cases) follow up sputum microscopy and the end of the intensive phase and at the end of treatment should be done. Response in patients with extra-pulmonary TB is best assessed clinically along with radiological and other investigations.

It is very important to do a drug sensitivity testing (DST) at time when the sputum smear is positive in follow up at any time during treatment. Rapid molecular DST as a first choice or culture DST at least for R resistance should be done. These are available free of cost in Intermediate Reference laboratories (IRL) all over the country and the sample can be sent through the district TB officer (DTO) who will further send it to IRL free of cost.

A very important change is the long term follow up of the patients who have completed the treatment. Clinical or sputum examination at the end of six or twelve months should be done.

DIAGNOSIS AND MANAGEMENT OF DR TB

Early diagnosis should be done for patients with presumptive MDRTB or DRTB in patients who have failed treatment of first line drugs, contacts of DRTB patients, patients who are sputum positive on any follow up, retreatment cases and TB patients with HIV co-infection. All these patients should be investigated for drug resistance preferably by rapid molecular testing. Wherever available DST should be considered and offered to all diagnosed tuberculosis patients prior to start of treatment. Patients with TB caused by drug resistant

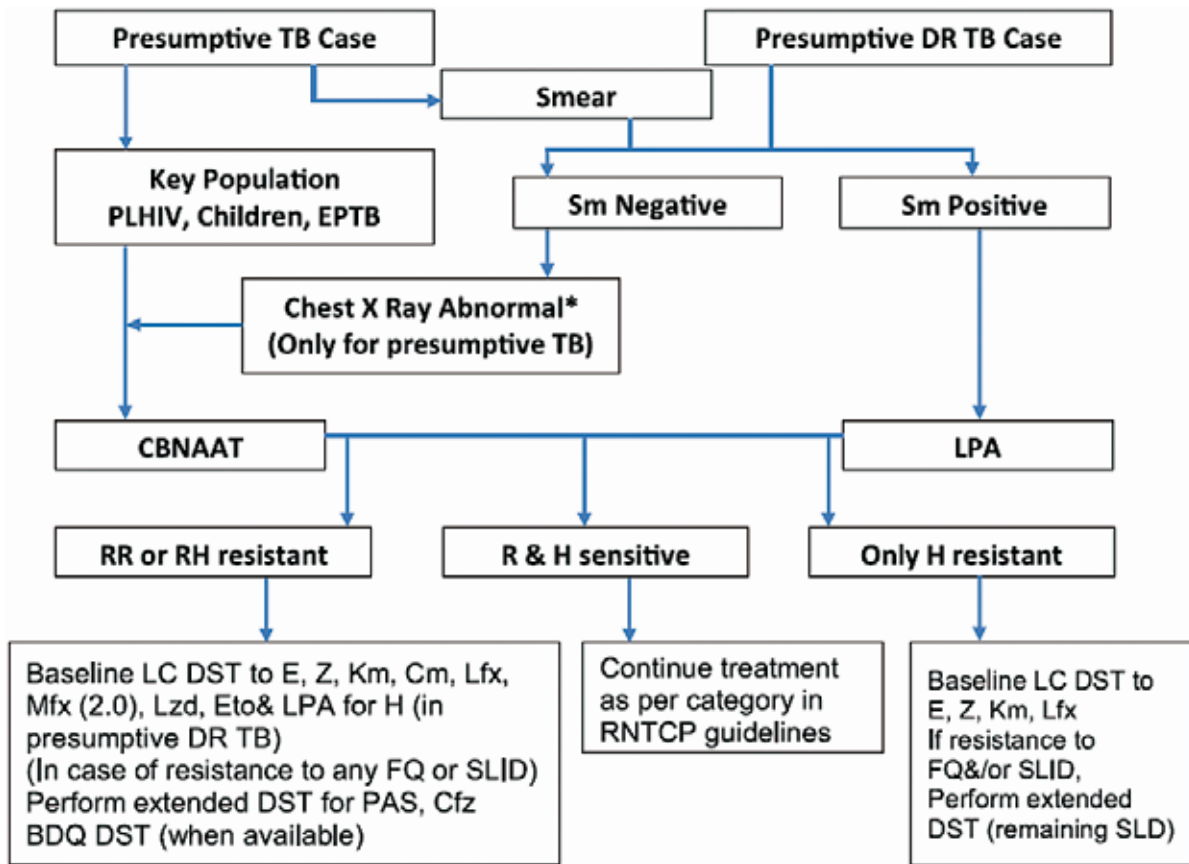


Fig. 4: Management of DR TB

organisms confirmed by an accredited laboratory should be treated with specialized regime with mainly ambulatory care. If required a short hospital stay is recommended. The diagnosis and management of DR TB patients is done free of cost under the RNTCP. The flow diagram helps in managing the DR TB patients (Figure 4).

The duration of treatment for newly diagnosed MDRTB patients should be at least 24 months out of which the IP should be six to nine months. The total duration can be changed as per the response of the patient.

XDRTB

If there is resistance to rifampicin and isoniazid all patients must be tested for second line DST in quality assured laboratories. All MDRTB isolates should be tested for Ofloxacin or Kanamycin resistance. The diagnosis and management of XDRTB should be under the expert guidance and it is available free of cost under the RNTCP programme.

CONTACT INVESTIGATION

All household and other contacts of the patients should be screened for TB. Reverse contact tracing should be done to search for any active case in the house where there is a case of paediatric TB.

ISONIAZID PROPHYLAXIS

Children <6 years of age who are in close contact of a TB patient should be given isoniazid prophylaxis for a minimum of 6 months after excluding active TB.

Since TB is now a notifiable disease by the government so to avail the free facilities available under the programme the coordination with DTO will be very helpful.

REFERENCES

1. <http://tbcindia.nic.in/>
2. Standards for TB care in India available for free download at <http://tbcindia.nic.in/>