Updated National Guidelines for Drug Susceptible Tuberculosis

LEBANON 2023

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Acknowledgment

The National Tuberculosis Program (NTP) of Lebanon is grateful and proud to announce that, despite the multifaceted crisis Lebanon is witnessing, we have succeeded to reach many of the targets set in the National Strategic Plan for TB Elimination 2017-2021, such as an incidence rate of 9.7/100000 population, a bacteriological confirmation of 90% among pulmonary TB cases and a treatment success rate exceeding 90% among Lebanese and refugees (*NTP Annual Report 2022)*.

These achievements were accomplished with the support of:
the World Health Organization
the International Organization for Migration through the generous grants of the global fund to fight TB, AIDS and Malaria.
the collective work of all our partners; the National TB Reference Lab "Laboratoire Rodolph Merieux" at Saint Joseph University, Fondation Merieux, the Armenian sanatorium / Azounieh, governmental hospitals, scientific societies, international and local NGOs and all health care providers.

And all of this wasn't possible without the dedication and hard work of the NTP health workers.

To be able to achieve the new targets set by the NSP to End TB in Lebanon (2023-2030) which goals and objectives focus on TB elimination in the country especially among DR TB and TB in children by 2030, NTP is calling you all for a multi-sectoral collaborative work based on a people centered equitable approach.

WE MUST ENSURE UNIVERSAL ACCESS TO TB SERVICES

National tuberculosis program manager

Dr Hiam Yaacoub

The updated National Guidelines for Drug Susceptible Tuberculosis-2023 were written by Alaaddine Walid MD, Yaacoub Hiam MD, Farhat Anne-Marie, Zgheib Joseph MD, Jradi Farah

Introduction

Despite the preventable and curable nature of Tuberculosis, the disease continues to be a public health threat globally with 10.6 million people who fell ill with TB in 2021, and it is the second leading cause of death from a single infectious agent, ranking after Covid19 and above HIV and AIDS with 1.6 million deaths globally in 2021.
Moreover, even with the new tools of very high quality, globally an estimated 4.2 million people were missed in 2021.

In Lebanon the TB detection rate remained relatively high and was estimated to 87% in 2021 in spite of the economic collapse witnessed by the country and its consequences such as poverty, malnutrition and poor access to the health services; These factors being important determinants of TB, a rise in TB cases is expected in the next couple of years.
Thus, the new NSP to end TB in Lebanon (2023-2030) which aimed to approach the TB pre-elimination phase by 2030 with an incidence of 20 case per million, had four objectives focusing on increasing the TB case detection rate, eliminating TB in children, eliminating DR-TB and improving the TBI cascade.

In alignment with the Lebanon National Health Strategy and the newly developed NSP to end TB in Lebanon, the National TB Program initiated the implementation of numerous interventions mainly aiming for:

- Integrating of TB services in governmental hospitals and Primary health care centers.
- Strengthening TB surveillance: through the development of district health information system(DHIS2) for TB and implementation in TB centers and national TB referral lab with a plan for expansion to the public and private hospitals, Contextualization of the WHO Prevent TB app for active case finding and screening in Lebanese prisons with a plan for expansion to the PHC and NGOs implementing the activity, LMS for drug distribution and stock management.

Based on the new evidences from clinical studies, new diagnostic tools, new drugs, updated international recommendations, the emerging situation in the country and the shift to an integrated service provision, The National Tuberculosis Program is updating the national guidelines for the management of drug susceptible TB, latent TB and TB in children.

Abbreviations & Acronyms

MTB	Mycobacterium Tuberculosis
DS TB	Drug susceptible Tuberculosis
Hr TB	Isoniazid resistant tuberculosis
RR-TB	Rifampicin-Resistant-Tuberculosis
MDR-TB	Multi Drug-Resistant Tuberculosis
PTB	Pulmonary Tuberculosis
EPTB	Extra-Pulmonary Tuberculosis
ITTB	Intrathoracic tuberculosis disease.
CXR	Chest Radiography (Chest X-ray)
CAD 4TB	Computer-Aided Detection of TB-related Abnormalities on Chest Radiography
DSM	Direct smear microscopy
MWRD	Molecular WHO-Recommended Rapid Diagnostic Test
NPA	Nasopharyngeal aspirate
PLWHIV	People living with HIV
ART	Antiretroviral Treatment
CRP	C-reactive protein
LF-LAM	Lateral Flow Urine Lipoarabinomannan Assay
DST	Drug susceptibility testing
IGRA	Interferon gamma release assay
TST	Tuberculin skin test
H	isoniazid
R	Rifampicin
P	Rifapentin

E	Ethambutol
Eto	Ethionamide
Z	Pyrazinamide
Mfx	Moxifloxacin
HPMZ	Shorter regimen treatment for drug sensitive tuberculosis (Isoniazid, Rifapentin, Moxifloxacin, Pyrazinamide).
TPT	TB Preventive Treatment
3HP	Three month TPT/weekly dose with Rifapentin + Isoniazid.
1HP	One month TPT/daily dose with Rifapentin+ Isoniazid
DHIS2	District Health Information System 2
Prevent TB App	application used for the registration in ACF actvities
LMS	Logistic Management Software
HBC	High Burden Countries
MOPH	Ministry of Public Health
NTP	National Tuberculosis Program
NTRL	National Tuberculosis Reference Laboratory
LRM	Laboratoire Rodolphe Merieux
IOM	UN agency for migration/international organization for migration
WHO	World Health Organization
NSP	National strategic plan
POD	prevention of disease
POI	prevention of infection
POR	prevention of disease recurrence

Latent Tuberculosis Infection and Tuberculosis Preventive Treatment

Definitions

Latent Tuberculosis infection is a state that is characterized by persistent immune response to stimulation by *Mycobacterium tuberculosis* antigens with no evidence of clinically manifest TB disease

Systematic Screening for Latent TB in Risk Groups

Risk group1 who should be screened for active and latent TB infection:

- Household and close contacts of the patients with pulmonary tuberculosis.
- PLWHIV: should be systematically screened for TB disease at each visit to a health facility.
- Immunocompromised individuals (other than PLWHIV): people taking immunosuppressive therapy including corticosteroids, with renal failure or on hemodialysis, with cancer, on chemotherapy, with organ transplantation.
- People with fibrotic lesion seen on chest X-ray and not treated for tuberculosis should be provided with TB preventive treatment after exclusion of the active disease.
- Prisoners: Before entering the prison and every two years.
- People who work in prisons: before their assignment and every two years.
- Migrant workers from high burden countries: on arrival to the country.
- Health care workers: at the start of their practice and then annually.
- Residents of elderly houses: annually.

Screening tools

TST or IGRA

- Two groups of contacts with bacteriologically confirmed pulmonary TB case, should receive TB preventive treatment/TPT after the exclusion of active TB, regardless of the result of TB infection test:
  - Children aged < 5 years.
  - PLWHIV at all ages.
- Migrant workers from high burden countries , who are newly arrived to Lebanon, should be tested by IGRA for two reasons:
  - IGRA is not affected by BCG vaccine (BCG vaccine is recommended and given in HBC).
  - According to the study conducted in Lebanon named " Towards an optimization in the screening strategy for Latent tuberculosis infection in different groups in Lebanon", where 40% of population tested positive by TB Skin test had negative IGRA test.
- All other risk groups above the age of 5 years may be tested either by TST or IGRA.

TB prevention

TB preventive treatment (TPT)

Should be offered only after exclusion of active TB in risk groups mentioned in this section.

TPT Protocols

- Isoniazid for 6 months for all ages
- Rifampicin for 4 months for all ages
- Rifampicin+ Isoniazid for 3 months for all ages
- 3HP (Rifapentin+ Isoniazid) weekly for 3 months for individuals> 5 years.
- 1HP (Rifapentin+ Isoniazid) daily for one month for individuals> 13 years.

TB Vaccination

TB Vaccination is an essential tool and future measure for TB prevention.
In fact, the 100 year-old BCG prevents only from severe TB forms in children below the age of two, is used in low burden countries and is not recommended for the general population.
After the long period of stagnation, many vaccines have recently been under study with three targets:
- POD = prevention of disease
- POI = prevention of infection
- POR = prevention of disease recurrence).

There are 16 vaccine candidates in clinical trials: four in Phase I, eight in Phase II and five in Phase III. They included candidates to prevent TB infection and TB disease, and to help improve the outcomes of treatment for TB disease.

Vaccines that are currently In phase III clinical trial

- MIP Whole-cell M. indicus pranii, POD.evaluating the efficacy, safety, and immunogenicity of MIP and VPM1002 (vs. placebo) in preventing TB disease (pulmonary or extrapulmonary) among 12,721 household contacts (≥6 years old, HIV negative) of people with TB in India .
- VPM1002 rBCG, POD,POI,POR, Undergoing a phase III trial evaluating the efficacy, safety, and immunogenicity of VPM1002 (vs. BCG) in preventing MTB infection among 6,940 newborns (HIV-exposed and uninfected eligible) in Gabon, Kenya, South Africa, Tanzania, and Uganda
- MTBVAC(live genetically attenuated MTB), POD, evaluating the efficacy, safety, and immunogenicity of MTBVAC (vs. BCG) in 6,960 HIV-unexposed and HIV-exposed, uninfected infants in South Africa, Senegal, and Madagascar.
- GamTBvac (Protein/adjuvant subunit Vaccine), in previously vaccinated with BCG. POD, Undergoing a phase III efficacy, safety, and immunogenicity study

of GamTBvac (vs. placebo) in preventing primary TB disease among 7,180 HIV-negative, BCG-vaccinated, MTB-uninfected adults aged 18–45 years in the Russian Federation.

- BCG (re) vaccination Whole-cell M. bovis, revaccination with BCG. POD,POI. Undergoing a phase III efficacy, safety, immunogenicity study of BCG revaccination vs. TB preventive treatment among 9,200 BCG-vaccinated, HIV-negative child and adolescent household contacts ages 6 to 18 years in India
- M72/AS01E (Protein/adjuvant subunit vaccine) POD in participant
- with MTB infection, was deemed to offer 54 percent protection based on the trial, conducted in Kenya, South Africa, and Zambia. this vaccine has received financial support for acceleration.

Active Drug Susceptible Tuberculosis

Definition(s)

Active Tuberculosis is a state of infection with mycobacterium Tuberculosis with clinical manifestation of the disease.

Active case finding (ACF) or systematic screening is a provider-initiated screening and testing for tuberculosis in high risk groups.

Active Case Finding in Groups at Higher Risk for Tuberculosis

This activity aims to:
- Preventing transmission of TB and, reducing the prevalence and the incidence of the disease as aligned with the strategic goal of TB elimination.
- Ensuring the early detection of TB, the prompt initiation of treatment and most importantly preventing advanced disease and deaths, improving treatment outcomes.

Risk group 1, who should be screened for active and latent TB infection:

- Household and close contacts of the patients with pulmonary tuberculosis.
- PLWHIV
- Immunocompromised individuals (other than PLWHIV): people taking immunosuppressive therapy including corticosteroids, with renal failure or on hemodialysis, with cancer, on chemotherapy, with organ transplantation.
- People with fibrotic lesion seen on chest X-ray and not treated for tuberculosis.
- Prisoners: Before entering the prison and every two years.
- People who work in prisons: before their assignment and every two years.
- Migrant workers from high burden countries: on arrival to the country.
- Health care workers: at the start of their practice and then annually.
- Residents of elderly houses: annually.

Risk group 2, who should be screened for active TB

- People with diabetes mellitus.
- People with chronic lung diseases.
- People who use drugs.
- Refugees living in crowded areas.

When to conduct the screening

- Household and close contacts of pulmonary TB patients: upon diagnosis of a pulmonary tuberculosis case.
- PLWHIV: should be systematically screened for active TB disease at each visit to a health facility.
- Immunocompromised individuals (other than PLWHIV): should be

systematically screened for TB disease at each visit to a health facility.
- People with fibrotic lesion seen on chest X-ray and not treated for tuberculosis should be screened systematically.
- Prisoners: Before entering the prison and every two years.
- People who work in prisons: before their assignment and every two years.
- Migrant workers from high burden countries: on arrival to the country.
- Health care workers: at the start of their practice and then annually.
- Residents of elderly houses: annually.
- People with diabetes mellitus, People with chronic lung diseases, people who use drugs and Refugees living in crowded areas may be screened periodically for active TB.

Screening tools

For latent tuberculosis infection (LTBI):
It is discussed in the previous section.

For active pulmonary tuberculosis:
- Symptom screening: (cough with any of the following symptoms: fever, weight loss, night sweats).
- In PLWHIV: symptom screening + CRP testing (cutoff > 5mg/l).
- Children < 10 years LWHIV should be screened for TB symptoms: any one of current cough, fever, poor weight gain or close contact with a TB patient.

Diagnosis

Pulmonary Tuberculosis:
- Chest x-ray: infiltrates in the upper lobes for pulmonary tuberculosis, Miliary patterns, pleural infusion, pericardial infusion, mediastinal lymph nodes.
- Computer-aided detection (CAD) is recommended for Chest X-Ray interpretation as an alternative method when digital X-ray is used, in adults and adolescents (older than 15 years).
- If Chest X-Ray findings are suggestive of tuberculosis, sample (sputum, BAL) should be tested by WHO recommended molecular testing (Gene-X-Pert Ultra, which detects mycobacterium tuberculosis and resistance to Rifampicin).
- Adults with X-Ray findings signs or/ and symptoms of pulmonary TB with a prior history of TB during the last 5 years should not be tested by Gene-Xpert (high possibility of false positive result).
- Patients intended to receive the new shorter 4-month (HPMZ) treatment for drug sensitive tuberculosis should be tested, in addition to Rifampicin resistance, for resistance to Isoniazid and fluoroquinolones on 10 colors Gene-

X-Pert and by phenotypic culture and DST for all TB drugs.

- In case Rifa resistance is detected, a second sample should be tested on 10 colors Gene-X-Pert (which detects MBT and resistance to Isoniazid and Quinolones).
- A third sample should be sent to the national TB referral lab for phenotypic and molecular drug susceptibility testing to other FLD & SLD (including new drugs: Bedaquilin, Linezolid, Clofazimin, Pretomanid).

Extra-Pulmonary Tuberculosis:

- A sample (Aspirate, biopsy….) should be tested by culture, which is more sensitive than pathology and PCR/Gene-x-pert.
- Samples from patients with life threatening forms of the disease (such as Meningitis, pericarditis, disseminated, contacts with MDRTB…) can be tested by Gene-x-pert to guide the prompt initiation of the treatment, however culture remain the gold standard.
- SOP for the preparation and handling of the samples will be attached as an annex to this guideline

Treatment protocols

6-months treatment

- Two months of Isoniazid+ Rifampicin+ Ethambutol+ Pyrazinamide followed by four months of Isoniazid+ Rifampicin (ERHZ/ 4RH).
- For pulmonary and extra pulmonary tuberculosis.

10-12 months treatment:

- Two months of Isoniazid+ Rifampicin+ Ethambutol+ Pyrazinamide followed by 7 to10-months of Isoniazid + Rifampicin (ERHZ/ 7-10 RH).
- For meningitis and osteo-articular, pericarditis. Corticosteroids to be added to the treatment for the first 6 to 8 weeks.

Shorter 4-months treatment "New Regimen"

- Two months of Isoniazid+ Rifapentin+ Pyrazinamide + Moxifloxacin followed by two months of Isoniazid+ Rifapentin+ Moxifloxacin.
- Dosage: Isoniazid 5 mg/kg, Rifapentin 1200mg, Moxifloxacin 400mg,pyrazinamide 25-30mg/kg
- Recommended for:
- Pulmonary tuberculosis.
- Adults and adolescents >12 years old.
- Individuals with weight> 40 kg.
- For cases without resistance to Rifampicin, Moxifloxacin, Isoniazid.
- Not recommended for:
- TB meningitis.
- Disseminated TB.

- Osteo-articular.
- People with low body weight (< 40 kg).
- Persons living with HIV infection with a CD4 count less than 100 cells/mm3.
- Pregnant, postpartum and breastfeeding women.
- Children 0-12 years.

In new pulmonary TB patients treated with the regimen containing rifampicin throughout treatment, if a positive sputum smear is found at completion of the intensive phase, the extension of the intensive phase is not recommended (strong recommendation, high certainty of evidence)

Treatments follow up

- Sputum test: direct smear microscopy on two samples at the end of month 2 of treatment, on one sample at month 5 and 6 of treatment.
- Chest X-Ray at the end of month 2 and at the end of treatment.

Adverse Events Monitoring

Allergic reaction

- Symptoms: rash, pruritus, Transient flushing reactions
- Management: It can be resolved without treatment in days, otherwise antihistamines should be prescribed, low dose corticosteroids if more serious.
- We have to stop all drugs till the symptoms disappear, and then
- Reintroduce TB drugs one by one every 3 days.
- When the responsible drug is identified, we stop it permanently and modify the treatment protocol accordingly.

Hepatotoxicity

- Symptoms: persistent nausea, vomiting or loss of appetite, jaundice, liver tenderness, hepatomegaly.
- Liver functions: If serum liver enzymes (ALT, AST) are more than five times the upper limit of normal, or more than three times the upper limit of normal with symptoms of hepatitis, hepatotoxic medicines should be stopped.
  Management:
- Liver enzymes monitored and the treatment resumed after they reach normal values.
- Drugs should be reintroduced one by one starting with Ethambutol and Rifampicin, followed by Isoniazid.
- Serum liver enzymes tests repeated in 3-7 days after the introduction of each drug.
- If they are normal with ERH, we continue with the three drugs for 9 months without pyrazinamide.
- If they increased again, the potential responsible drug should be stopped and

substituted (For example If Rifa is the responsible drug, we treat with ethambutol, Cycloserin, Linezolid and a Fluoroquinolone).

- If severe hepatotoxicity occurs during the continuation phase with RH, treatment can be stopped if patient has already received 80% of the treatment, or treated with ethambutol, Cycloserin, linezolid and a fluoroquinolone if less than 80% were received.

Peripheral neuropathy

- The responsible drug is Isoniazid, may cause symptomatic pyridoxine (vitamin B6) deficiency.
- Symptoms: pain, burning or tingling in the hands or feet, numbness or loss of sensation in the arms and legs, muscle cramps.
- Management: Supplemental pyridoxine is recommended.

Optic Neuritis

- The responsible drug is Ethambutol.
- It is very low for treatment duration of 2 months, and ethambutol should be used in TB treatment regimens in children of all ages as per WHO recommendations .
- If diagnosed, ethambutol should be omitted from the regimen.

Treatment of patients with renal impairment/dialysis.

- No need of dose adjustment for Rifampicin and Isoniazid,
- Ethambutol and Pyrazinamide to be prescribed at the lower dose of recommended when creatinine clearance is less than 30ml/min or three times/week at the recommended doses.
- For patients on dialysis: three times per week after the dialysis session.

Drug Susceptible Tuberculosis in Children

Definition(s)

Pulmonary Tuberculosis in children

- The lung parenchyma is affected (infiltrates…).
- Miliary TB.
- Intrathoracic lymph nodes.

Screening

Risk groups

- Children contacts with pulmonary TB.
- Children living with HIV.
- Reverse contact screening: When a child is diagnosed with any form of tuberculosis, his/her close contacts should be screened for active tuberculosis aiming to find the source of the infection.

Screening tools

- Symptom screening: any symptom such as current cough, fever, poor weight gain, close contact of an individual with pulmonary tuberculosis.
- Symptoms of extra pulmonary TB: cervical lymph nodes, symptoms of Meningitis (vomiting, unconsciousness or sleepiness…).
- Tuberculin skin test (TST/PPD): induration of ≥ 10 mm, > 5 mm in children LWHIV.

Diagnosis

Chest x-ray should be performed for those, who tested positive by any of the listed above screening tools.
Bacteriological confirmation should be sought as part of the integrated treatment decision algorithms whenever possible.

TB Testing

Gene-x-pert and Culture

Type of Samples

- Sputum, gastric and nasopharyngeal aspirates should be tested by Genexpert and culture.
- Stool should be tested by Genexpert.
- FNA from a Lymph node by Genexpert and culture.
- Biopsy sample by culture.
- Aspirate in pleural effusion, ascites and all other effusion to be tested by culture.
- Cerebrospinal fluid to be tested by Genexpert (to guide early treatment initiation) and culture.

Treatment protocols

An integrated treatment decision algorithm should be implemented, based on a combination of diagnostic tests, chest radiography and clinical signs and symptoms.

4-months treatment regimen

- Two months with Isoniazid Rifampicin+ Pyrazinamide+ Ethambutol, followed by Two months with Isoniazid+ Rifampicin (2HRZ (E)/2HR).
- Recommended for children between the age of 3 months and 16 years with non- severe form of TB and without suspicion or evidence of resistant tuberculosis, including children and adolescents living with HIV.
- Non severe forms: Peripheral lymph node TB, intrathoracic lymph node TB without airway obstruction, pulmonary tuberculosis localized in one lobe without cavitary lesion, without dissemination, no miliary pattern, non-complicated pleural effusion.

6-months treatment regimen

- (2HRZ(E)/4HR) recommended in severe forms
- Disseminated TB, osteo- articular TB, peritonitis, pericarditis, renal, spinal.
- For children < 3 months of age, with weight less than 3 kgs.
- For children with acute malnutrition.
- In children and adolescents with bacteriologically confirmed or clinically diagnosed TB

Treatments for Meningitis (without suspicion or evidence of MDR/RR-TB)

- 12-months: (2HRZ(E)/10 HR).
- 6-month intensive regimen with Isoniazid+ Rifampicin+ Pyrazinamide+ Ethionamide (6HRZEto) may be used as an alternative option to the 12-month regimen (2HRZE/10HR).
- Corticosteroids should be used in the first 6-8 weeks, as part of the treatment for TB meningitis; and may be used for the treatment of tuberculous pericarditis.

Other conditions:

- Infants aged <3 months or weighing <3 kg: pulmonary TB of any severity should receive the 6-months treatment 2RHZ (E)/4RH.
- Children with malnutrition, infants aged less than 3 months, and children treated for TB in the past 2 years are not eligible for the 4-month regimen and should be treated with the 6-month regimen.

Treatment Failure in children

- Has no symptom resolution or has worsening of symptoms;
- Shows continued weight loss;
- Smear-positive at 2-months' follow-up (for children and adolescent with bacteriological confirmation at diagnosis).

Recommended dosages of first-line TB medicines for use in children and young adolescents aged 0–14 years

(excluding TB meningitis treated with alternative short intensive regimen)

Medicine	**Dose (mg/kg body weight)**	**Range (mg/kg body weight**
Isoniazid (H)	10	7–15 a
Rifampicin (R)	15	10-20
Pyrazinamide (Z)	35	30–40
Ethambutol (E)	20	15–25

Dosing table for first-line medicines for Fixed dose combination drugs

Weight (kg)	**Number of tablets a**		
	Intensive phase: HRZ 50/75/150 mg	**E 100 mg b**	**Continuation phase: HR 50/75 mg**
4–<8	1	1	1
8–<12	2	2	2
12–<16	3	3	3
16–<25	4	4	4
≥25	Adult dosages recommended		

Management of treatment interruption in children and adolescents

Treatment interruption	Details of interruption	Management
Intensive phase		
Intensive phase: applies to 4- and 6-month regimens	Interruption <14 days	Continue treatment and complete all intensive phase doses
	Interruption ≥ 14 days	Restart intensive phase
Continuation phase (4-month 2HRZ(E)/2HR regimen)		
Continuation phase (4-month regimen)	Completed ≥80% of doses within 8 weeks	Further treatment not necessary
Continuation phase (4-month regimen)	Completed <80% of doses and cumulative interruption <1 month	Complete remaining doses of treatment
Continuation phase (4-month regimen)	Completed <80% of doses and cumulative interruption >1 month	Restart treatment from beginning of intensive phase
Continuation phase (6-month 2HRZE/4HR regimen)		
Continuation phase (6-month regimen) and bacteriologically negative at initiation	Completed ≥80% of doses within 16 weeks	Further treatment not necessary
Continuation phase (6-month regimen) and bacteriologically positive at initiation	Completed ≥80% of doses within 16 weeks	Complete remaining doses of treatment If consecutive lapse is >2 months, use clinical judgement
Continuation phase (6-month regimen)	Completed <80% of doses and cumulative interruption <2 months	Complete remaining doses of treatment
Continuation phase (6-month regimen)	Completed <80% of doses and cumulative interruption ≥2 months	Restart treatment from beginning of intensive phase, particularly if interruption was consecutive

Prevention

Children eligible for Tuberculosis preventive treatment (TPT):

- Children contacts with pulmonary tuberculosis regardless of TST result and in whom active tuberculosis is excluded.
- Children living with HIV regardless of TST result and in whom active tuberculosis is excluded.

TPT protocols

- Isoniazid (H) for 6 months, 10mg/kg/day with 300mg as a maximum dose.
- Rifampicin (R) for 4 months, 15 mg/kg/day.
- Isoniazid and Rifampicin (RH) for 4 months.
- HP once a week 3 months.
- HP daily for one month.

<table>
<tr><td rowspan="8">Three months of Rifapentine plus isoniazid weekly (12 doses) (3HP)</td><td colspan="6">Age 2–14 years</td></tr>
<tr><td>Medicine, formulation</td><td>10–15 kg</td><td>16–23 kg</td><td>24–30 kg</td><td>31–34 kg</td><td>>34 kg</td></tr>
<tr><td>Isoniazid, 100 mg*</td><td>3</td><td>5</td><td>6</td><td>7</td><td>7</td></tr>
<tr><td>Rifapentine, 150 mg</td><td>2</td><td>3</td><td>4</td><td>5</td><td>5</td></tr>
<tr><td colspan="6">Age >14 years</td></tr>
<tr><td>Medicine, formulation</td><td>30–35 kg</td><td>36–45 kg</td><td>46–55 kg</td><td>56–70 kg</td><td>>70 kg</td></tr>
<tr><td>Isoniazid, 300 mg</td><td>3</td><td>3</td><td>3</td><td>3</td><td>3</td></tr>
<tr><td>Rifapentine, 150 mg</td><td>6</td><td>6</td><td>6</td><td>6</td><td>6</td></tr>
<tr><td colspan="6">* 300mg formulation can be used to reduce pill burden</td></tr>
</table>

Drug Susceptible TB and HIV

TB is the most frequent cause of deaths in people living with HIV, with one third of deaths in PLWHIV are due to TB.
The risk of TB in PLWHIV is strongly associated with the level of immunodeficiency, which increases with the progression of the immunosuppression from 2-5 to 20 fold compared to HIV negative population.
Antiretroviral therapy (ART) does not fully restore the baseline level of risk.
Clinical presentation is similar to non HIV with pulmonary form, when 50/ µL<CD4 T cells count< 350/µL.
Extra pulmonary form is more common with the progression of the immunosuppression (CD4 less than 50/µL).

Screening

For active TB: Symptom screening and C reactive protein (CRP) in new tested HIV positive and still not on anti-retroviral therapy.

Diagnosis

- Gene-Xpert should be used for PTB as a first test, followed by the culture,
- Blood culture may be considered, in the advance stage of HIV disease where the bacteriological confirmation will be difficult because of the paucibacillarity and because of the fact that EPTB form is more common.

Treatment

- 2 months ERHZ/ 4months RH,
- Recommended to start ARV treatment within the first two weeks of TB treatment regardless of the CD4 count,

Same duration of treatment as HIV negative TB patients..

- In case of TB meningitis, ARV should be delayed for at least four weeks, so that the risk of severe neurological TB-IRIS may be treated with glucocorticoids.
- Shorter 4 month new regimen – HPZM can be used when CD4 count is ≥ 100 cells/mm3.

Latent TB

Current tests for TBI have a lower sensitivity in people with advanced HIV, and according to the WHO, all HIV-infected individuals should receive TPT irrespective of the TBI test result. However, the yield of TBI screening and TPT in low TB-endemic settings is currently unknown, Studies showed more decline in occurrence of active TB in people with positive TST (64% compare to 30% in those with negative TST).
Based on the above it will be recommended in our settings to:
- Provide TPT to PLWHIV, who were in contact with pulmonary TB regardless of TB tests after the exclusion of active TB disease.
- Test PLWHIV (other than the contacts of PTB cases) for latent TB infection with either TST or IGRA, and provide TPT for those with positive result after the exclusion of active TB disease.

Drug Susceptible TB and Diabetes:

- It was estimated that 15% of people with TB have diabetes globally in 2019, compared with 9.3% among the general adult population.
- TB does not cause DM; however some studies showed that up to 50% of TB patients have transient stress-induced hyperglycemia. Patients with such type of diabetes may still be at higher risk of future diabetes (similar to gestational DM).
- Diabetes is associated with a 2-3 fold risk of TB disease, and a higher risk of multidrug-resistant TB (MDR-TB).
- Diabetes is associated with more pulmonary cavities and a higher bacterial load according to some studies.
- Diagnostic approaches are similar to those for patients without DM.
- TB-DM, TB treatment is similar but toxicity or dangerous drug interactions are more common.
- Delays in microbiological responses, associated with increased rates of death, failure and relapse.
- Higher risk of treatment failure, relapse and death.
- TB screening is not recommended in patients with diabetes in Lebanon as all countries with low TB incidence.
- TPT is not recommended for DM patients.
- All TB patients should be tested for diabetes by asking about having diabetes and a simple fasting blood glucose test.
- Repeat the test at the end of TB treatment to exclude or confirm diabetes.

TB in prisons

Many reasons are behind the strong recommendation for TB screening in prisons:

- Prisoners are one of vulnerable population with poor access to the health care system.
- The estimated incidence of TB among prisoners is 23 times higher than that among the general population,
- Some studies showed that screening in prisons improves early case detection, increase overall case detection and reduce TB prevalence.

Tools

Prisoners should be screened for active and latent TB:

- New comers: by symptoms, TST and Chest X-Ray.
- Old residents: by Symptoms and TST.
- New assigned staff to work in prisons: by symptoms, TST and Chest X-Ray.
- Old staff working in prisons: biennially by Symptoms and TST.

Diagnosis

Algorithm for diagnosis is the same as all other presumptive TB cases outside the prisons.

Treatment

Protocols are designed according to the medical conditions as in other groups.

Infection control

To reduce the transmission of M. tuberculosis, the following measures are recommended:

- Respiratory separation/isolation of people with presumed or confirmed infectious TB.
- Prompt initiation of effective TB treatment of people with TB disease.
- Respiratory hygiene including cough etiquette, sputum collection in people with presumed or confirmed TB.
- Upper-room germicidal ultraviolet systems are recommended to reduce M. tuberculosis transmission to health workers, persons attending health care facilities.
- Ventilation systems: natural, mechanical ventilation and recirculated air through high-efficiency particulate air (HEPA filters).
- Surgical mask for TB patients.
- Respirators: N95 mask for health care workers.

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