rGLC report format

TECHNICAL ASSITANCE REPORT

Country:	Myanmar
Dates of TA provision:	8th & 9th June 2020
Consultant(s):	Dr.C.Padmapriyadarsini
Clearance of the report	The content of the report has been fully cleared by the National Tuberculosis Program, Myanmar
Sharing of the report	1. The report has been shared with The Global Fund Portfolio Manager, Myanmar and the TGF GLC Focal Point. 2. In-country circulation of the report done via WHO Country office in Myanmar
TA coordination	rGLC/SEAR Secretariat and WHO Country office Myanmar
Summary of the TA provided	In Myanmar, about 2,800 MDR/RR-TB patients are started on treatment each year and treatment success rate is 80% among MDR-TB. The new anti-TB drugs (bedaquiline and delamanid) and shorter treatment regimen (STR) have also been introduced in various regions of Myanmar for eligible DR-TB patients under the NTP and the endTB Project and high treatment success rates (>80%) amongst initial cohort of DR-TB patients treated with the STR, has been reported by the rGLC. Second line anti TB drugs, including the newer anti-TB drugs have side effects and active drug safety, monitoring (aDSM) and management must be done for patients' safety. Diabetes mellitus can significantly increase the odds of developing MDR-TB. Consequently, a more robust TB treatment and follow-up might be necessary for patients with DM. Efforts to control DM can have a substantial beneficial effect on TB outcomes, particularly in the case of MDR-TB. In Myanmar the prevalence of diabetes mellitus is approximately 7% while the prevalence of risk factors are high (17% are overweight and 9% are physically inactive). Trainings on the Active Drug Safety Monitoring and MDR-TB with Diabetes mellitus were held virtually on June 8th & 9th, 2020. Approximately 150 participants attended the training. The training was a comprehensive overview of aDSM and DM-MDR TB and covered the following topics and key concepts: <u>aDSM</u>: 1. Introduction and Definition : Various terminologies of adverse events, adverse drug reaction, adverse event of clinical significance were explained 2. Serious Adverse Events (SAE): The 6 characteristics to identify SAE, grading the severity, relatedness and expectedness were discussed in detail along with examples 3. Causality assessment: Methods to assess the causality of serious adverse events were discussed. Time relationship, pharmacological characteristics, medical plausibility, ruling out other causes, dechallenge and rechallenge of drugs were addressed and explained

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4. WHO UMC category for classifying casuality assessment was discussed in detail. It was discussed as to how to identify the causality criteria as certain, probable, possible or unlikely
5. It is advisable to follow a clinical and laboratory testing schedule for aDSM assessment which may be adapted depending on the regimen given to the patient, as per the national guideline. It should be a guidance document and should show the very minimum to be done for any adverse event till normalisation is reached
6. Assessing and managing Adverse events during MDR-TB treatment were discussed. WHO's rapid communication of Dec 2019 on DR-TB treatment and Principles of designing WHO all oral longer regimen were briefly discussed. All known AE were briefly enumerated.
7. Detailed discussion with case study and causality assessment were done for (i) visual disturbances (ii) peripheral neuropathy (iii) QT prolongation (iv) myelosuppression (v) hepatitis. Other adverse events like hypokalemia, hypothyroidism, vomiting and abdominal pain were touched upon
8. Drug replacement principles and sequence of replacement as followed in Indian PMDT guidelines were discussed. There was some discussion from the audience on this as this was different from that being followed in Myanmar. The reason of the sequence of replacement in Indian guidelines were explained.

<u>DM-MDR TB</u>

1. Various studies highlighting the increased risk of individuals with diabetes mellitus of developing active TB were enumerated. Individuals with Diabetes mellitus has two times increased risk of developing drug resistant TB.
2. When to screen for DM in TB patients: TB patients should be screened for DM at the time of diagnosis and registration. Those with blood glucose consistent with pre-DM or DM should all be re-tested at the end of TB treatment and a decision made at that time on future management
3. We discussed how to identify the different categories based on the blood glucose levels for impaired glucose tolerance, pre-diabetes and diabetes mellitus
4. Based on the screening result, how to manage the (i) newly diagnosed diabetic TB patient or (ii) already known diabetic patient.
5. Monitoring of glucose control during TB treatment is best done by measurement of FBG. HbA1c can be used but is generally not repeated within 2-3 months after starting DM treatment
6. Common glucose lowering agents that can be used with anti-TB drugs were shown along with their starting dose, interaction with anti-TB drugs, main side effects and dosing with reduced GFR, in a tabular format
7. Case studies were discussed on identification and management of MDR-TB patient with diabetes mellitus comorbidity
8. It was emphasized not to delay initiating treatment for the want of diabetologist. It was reiterated to initiate treatment for diabetes mellitus at the TB care centre itself and can be subsequently adjusted with a diabetologist consult, if there is a need.
9. Drug-drug interaction, adverse events and therapeutic drug monitoring were also briefly discussed
10. DM appears not to be a risk factor for unfavorable outcomes in DR-TB patients
11. The whole presentation emphasized on *"one patient – one health care worker – one health system – two (or more) diseases*"

Summary of the recommendations to follow up	<u>aDSM</u> • Adverse events are common and are to be expected during treatment for DR-TB • Routine monitoring is important for all patients on MDR-TB treatment; aDSM is the systematic way of achieving this • Early recognition and optimal management of adverse events is key to ensuring better treatment outcomes • Standard scales can help with severity ratings and finding the appropriate management option • Health care providers need to be trained and supported to provide appropriate care – including management of adverse reactions – to patients <u>DM-MDR TB</u> • Diabetes Mellitus : an independent risk factor for MDR-TB (esp primary MDR) • All people with TB should be systematically screened for DM • Consider Targeted screening of TB patients (> 40 years of age) for DM • DM patients should be offered systematic screening for TB only in high-TB burden countries where TB prevalence is > 100 per 100,000 people • FBG and HbA1c are the preferred diagnostic tests for DM in patients with TB • In persons with already established DM, there should be a heightened index of suspicion of TB and test for TB if suggestive symptoms and signs are present • Patients with DM and TB need to be counselled about appropriate lifestyle management (smoking cessation, good diet and physical activity). • Treatment for drug-susceptible and drug-resistant TB is similar in persons with and without DM • Health workers should be vigilant about monitoring treatment response as treatment failure and recurrent TB are more common in persons with DM. • People with both DM and infectious TB should be treated for at least the first two weeks and preferably the first two months just in the TB clinic • Visits to the DM clinic should be avoided wherever possible to prevent the transmission of *M.tb* to health workers and persons with DM in that setting • *Metformin* is the first-line drug of choice for treating persons with DM if medication is needed to control elevated glucose levels • Insulin may have to be considered if blood glucose levels are very high or in those whose blood glucose levels are not controlled with oral hypoglycaemic drugs. • Efforts to control DM can have a substantial beneficial effect on TB outcomes, particularly in the case of MDR-TB.

rGLC comments: Follow-up to measure effectiveness of such trainings.

Action items for the programme to

1. actively monitor for aDSM and ensure timely review and change of treatment regimen, if needed.
2. DM screening among MDR-TB patients for timely DM treatment. NTP can track outcomes of DM-TB patients to see if there is an impact.