rGLC report format

TECHNICAL ASSITANCE REPORT

Country:	Nepal
Dates of TA provision:	From 24th June to 26th June 2020
Consultant(s):	Dr Asif Muhammad
Clearance of the report	The content of the report has been fully cleared by the National Tuberculosis Program, Nepal and WHO country Office, Nepal.
Sharing of the report	1. The Director of NTCC and his team 2. In-country circulation of the report done via WHO Country office in Nepal 3. TGF Country Portfolio manager through WHO-SEARO
TA coordination	rGLC/SEAR Secretariat and WHO Country office Nepal
Summary of the TA provided	With the support of WHO rGLC/SEAR Secretariat office New Delhi, in close coordination with WHO Country Office, Nepal and with guidance and under the leadership of the National TB Control Center, Nepal, the TOT on Programmatic and Clinical management of DR-TB was provided virtually. The application used for training was Microsoft Team. There was diversity of participants including TB Consultants and clinicians, PMDT physicians, physicians from partner organizations, coordinators from all over the country reaching to a total number 26 in TOT. While, the facilitators from within the country were also included in training delivery. The whole training was recorded and can be accessed any time on request to NTCC and WHO country office, Nepal. The NTCC Director, Nepal welcomed and addressed to all participants and emphasized on components of PMDT management and active participation in the training. He also expressed his gratitude the WHO SEAR Office, WHO Country Office for this support despite COVID-19 situation. While WHO Country Office Team Lead and I also appreciated the Nepal NTCC as Nepal is among the 1st countries globally to take initiatives to start all oral regimens nationwide. Likewise, such virtual TOT on new WHO/ NTCC guidelines is also the 1st of its kind which was held in Nepal and could be good example for other countries in the region. Overall, the training mode was kept much inclusive with actively engaging participants by asking questions, case discussions during presentation and case scenarios as best practice examples. The following topics were covered during the National TOT on Programmatic and Clinical Management of DR TB (TOT agenda is attached); 1. Introduction of all participants and facilitators followed by Pretest taken by all participants which lasted for 25 minutes. 2. As per 2018/19 Prev. survey data, TB prevalence and incidence are 416 and 245 per 100,000 population and TB cases notified in 2018 are 32043 and about 54% TB cases missing with about 3% annual TB case reduction. There is diversity among notified cases, 36% of female and 64% of male cases were notified. Regarding MDR TB during the last 5 years, an average of 334 RR/MDR TB cases have been enrolled with rapid scale up of SSTR in the recent years. Moreover, there is 55% gap in RR TB estimated and notified, while the gap in notified and enrollment cases is around 62%. The TSR

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among SSTR cohort is 65%, LTR cohort is 71% and for XDR TB cohort 88%. The FQ resistance reported in the country among RR TB is around 36% and XDR TB is 7%.

3. As this was TOT, presentation on basic training provision skills and it was emphasized that how a good training is helpful in bridging the existing skills and knowledge to transform, update and enhance skills and knowledge.
4. The training covered all aspect of diagnosis of TB/DR TB, interoperation of the Xpert and LPA results at filed level and clinical implications. Three facilitators covered this topic from various aspects of diagnosis.
5. The Medical Officer MDR TB from WHO SEAR office comprehensively updated on WHO consolidated guidelines on tuberculosis – drug-resistant TB treatment and evidence summary on reclassification of drugs in WHO new guidelines.
6. The topic of treatment strategies of RR/MDR TB, RR TB with additional resistance, management of RR/MDR TB failures and relapses were also covered with discussions and case examples. As per Nepal NTCC DR TB updated guidelines the regimens LR1, LR2, LR3, LR4, keeping in view the different scenarios were discussed and emphasized. The focus was made on early and timely detection of Lzd and Bdq related toxicities as these drugs will be largely scaled up nationwide where staff might have less experience of using them. The participants had lot of questions and debates on selection of appropriate regimen in COVOD lockdown situation and when SLPA results are significantly delayed/ not available. The proposed solutions are given in recommendations section below.
7. The component of SSTR with Bdq containing regimen was updated and shared with WHO country office and NTCC week before training and protocols of SSTR with Bdq containing regimen were presented and its implications and management and discussed thoroughly for future consideration.
8. Likewise, the detection and diagnosis of Hr TB was also discussed in line with WHO new recommendations and the updated NTCC guidelines. However, it was also covered that how to manage when there is Lfx resistance with Hr TB and cases who failed Cat1 treatment and use of likely effective drugs in the regimen with Hr+ TB.
9. Similarly, the section on Childhood DR TB diagnosis and management was also covered as part of the training. The emphasis was on importance of childhood TB detection by using definitions of confirmed, probable and possible DR TB in children. The treatment of children with all oral regimen by using Bdq, DLm as per defined and recommended age category with possible duration from 9-12 months in most cases by using pediatric formulation as priority. Likewise, the management of RR/MDR TB in Pregnancy and meningitis was also covered along with brief discussions.
10. The aDSM component was highlighted as essential component of PMDT for all RR/MDR/Pre-XDR/XDR TB patients throughout, including presentations on application and implementation, strengthening and scaling up aDSM nationwide. Likewise, the element and benefits of causality assessment was also emphasized. Moreover, the topic of detection and management of mild to severe side effects (AEs, SAEs) was also imparted during the training.
11. The presentation on Monitoring and Evaluation of PMDT along with R&R was delivered by NTCC M&E Specialist where all components and importance of data entry and reporting as per NTCC protocols were highlighted and discussed thoroughly.
12. Posttest was taken by all participants at the end of training

At the end of the three days training, the NTCC Director, WHO country Office, Chief of Planning NTCC and PMDT Chief along with WHO Nepal Office CDC Team Lead and WHO SEAR, MO delivered the conclusion remarks. In addition, the feedback from participants was also taken for the 3 days MDR TB TOT. All of them appreciated to conduct this useful

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TOT and is a key for practice shift from Injection to all oral regimens in Nepal and also setting an example and a precedent for holding the virtual TOT on PMDT in the region. This training was also an example of an excellent team work of NTCC, WHO country Office, The PR- Save the Children, Damian foundation, all the DR TB treatment centers, WHO-SEARO and r-GLC member (Lead facilitator). This training can be replicated in other countries in the context of COVID-19 situation.

Training Evaluation

It was pertinent to evaluate training as per training norms. The pre and post test was performed and the results in below table are showing significant improvement when the pre training test and post training tests were evaluated.

Table: Pre and Post test results

Tests	Correct answer %
Pre-test	55%
Post-test	71%

Summary of the recommendations to follow up

Based on presentation on TB epidemiology delivered by Chief planning NTCC, overall, the country achievements are appreciable with fairly good TSRs both in DS and DR TB. The new NSP is covering all the elements of End TB strategy with well defined goals and objectives.

Background of PMDT & Diagnostic Facilities

TB and PMDT Facilities :4382 DOTC centers- 21 DR TB treatment centers- 81, DR TB subcenters- 6 DR TB hostels and 4 DR TB referral centers

Diagnostic Facilities: Microscopy Centers 604- G.Xpert machines 76-CL/DST Labs 2(3 under plan)

On the basis of observations from Power point and discussions during training delivery following recommendations are made;

Recommendations:

1. Reduce the gap between estimated and notified cases both for DS TB(54%) and DR TB(55%) in the country and address this appropriately and to reach the unreached population including addressing diversity in male and female cases notified.
2. The treatment success rates (TSR for DR TB are optimistic as compare to global trends. However, following needs to be looked in to because of significant difference in DR TB cohort wise TSR;
   2.1. SSTR cohort is 65%, LTR cohort is 71% and for XDR TB cohort 88%. Though his could be due to low number in LTR and XDR TB cohort, but still it will be great to evaluate for low TSR in SSTR and very high TSR in XDR TB.
   2.2. For SSTR cohort, evaluation should be carried out that is there any amplification of resistance for FQ during treatment, comparison of LTFUP between LTR and SSTR and also failure rate among two regimens.
3. Other components, like gap between RR TB notified and enrolled is 62%(initial lost to follow up), Lost to follow up during treatment is about 9%, which is high in such low number of cases of DR TB (about 330 yearly) in the country. Addressing this high number is extremely important on priority thorough decentralizing the DR TB care, education and counselling to staff, patients and DOT providers, strengthening linkages between DOTS centers, PMDT and xpert sites and, strengthening monitoring. Also, not to rely only on G.xpert notifications but also should be verified by monitoring the receding and reporting of RR TB cases notified and enrolled.
4. Strengthening intervention of sample transportation for SL LPA/DST as in some regions samples may not be reaching to the labs for testing due to not having the sample transport services.

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5. Reducing the Turnaround time (TAT) for SL LPA results which is currently ranging from 10 days to 6 weeks (depending upon region to region) to 7-10 days. Delays in SL LPA results and or not having testing of SL LPA may have strong impact on SSTR and overall, on DR TB outcomes due to underline FQ resistance (36%) which is high in country.
6. If possible further decentralization of SLLPA labs while maintaining the quality
7. The Pre XDR (FQ resistance) is fairly high in the country mounting to 36%, which is a worrisome matter to place patients on SSTR particularly when Bdq based SSTR will be used. This is particularly emphasized because of either significant delay in SL LPA results or not available in some cases and high underline FQ resistance may amplify resistance to other drugs (specially to Bdq/Cfz).
8. There was debate on appropriate regimen during COVID lockdown situation, SL LPA results significantly delayed or not available, monitoring CLs cannot be done. Similarly, country has high FQ resistant among RR/MDR TB cases (36%). In such situations and country context following regimen options may cover some cases with underline FQ resistance until DST results are available. Following is proposed for empirical regimen to use;

    Option 1- Commence patients in these situations on LR1- 18Lfx,Bdq(6), Lzd, Cfz, Z and then once if SL LPA shows FQ susceptibility then switch to SSTR by removing Lzd and adding Eto, INHh and E- **BUT**, this should be done with in 28 days of treatment initiation. If, FQ resistance then modify as per FQ resistance regimen per guidelines. *(Ref: WHO Operational handbook 2020)*

    Option 2. 18 Lfx,Bdq(6),Lzd, Cfz, Cs this may cover underline high FQ resistance prevalence situations, but still SL LPA for FQ is always mandatory
9. NTRL should make efforts for baseline DST testing for Bdq and if any Positive CL is reported during treatment should also be subject to SL LPA for FQ and DST to Bdq. Meanwhile isolates of positive CL during treatment may be sent to SNRL or abroad for testing for Bdq resistance.
10. Strengthening and scaling up aDSM with causality assessment
11. Pediatric TB/DR TB diagnosis and treatment should be addressed on priority in the country
12. A follow up face to face training later on to further strengthen capacity of management of PMDT

Operational Research

1. Nepal NTCC and WHO country office can discuss conducting OR for modified SSTR in line with discussions with WHO SEAR and the regimen to be used under OR should address the high FQ resistance prevalence in the country. One of the examples could be to add Lzd (for 2 months or until SL LPA/DST result is available) in regimen instead of E and change back to E and take out Lzd once DST to FQ is available and susceptible. If FQ resistance reported switch to Pre XDR TB treatment as per guideline. Moreover, country can also follow and adopt the mSSTR operational research protocols already available. Moreover, the TDR ShORRT package can also be used.
2. As WHO has recommended BPaL under operational research for XDR, Pre XDR and where no other option is left to compose effective regimen, therefore, Nepal NTCC can plan for BPaL under Operation al research as country may be benefited from BPaL

Acknowledgments:

The gratitude and gratefulness goes to following personal/ organizations for their tremendous support, efforts and coordination which enabled this TOT to happen in country;

	1. The Director of NTCC Nepal, Chief of Planning and Research NTCC, Chief of PMDT, Nepal and NTCC team for Leadership and support 2. WHO country office CDC team lead and team members for their continuous support and efforts to make this training happen. 3. WHO SEAR Office TB/MDR TB Unit team, specially to WHO Medical Officer MDR TB 4. In country Save the Children office colleague and colleagues from GENETUP and Damien foundation for their support

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Agenda of TOT on Programmatic and Clinical Management of DR-TB-Kathmandu-Nepal

Dates: 24th – 26th June 2020

Mode of Training: Virtual Training

Methods of Training: Powerpoint Presentations, Interactive methods between Participants and Trainer, Case Studies, Transforming Problem solving skills from examples of real practice of PMDT

Training Objectives:

- To update participants on National revised and updated PMDT guidelines as per WHO new recommendations
- Induct, prepare and training for trainers on PMDT for capacity building across the country
- Transfer knowledge and develop in-depth understanding to increase the knowledge on DR TB prevention, diagnosis and various aspects of clinical and programmatic management of DR TB

Key facilitator

1. Dr. Asif Muhammad
   MD.MPH(UK), DTM&H(UK), Dip Diabetes(South Wales), Senior Advisor MDR TB to NTP Myanmar
2. Dr. Vineet Bhatia
   Medical Officer MDR-TB, Department of Communicable Diseases, WHO, SEAR office
3. Dr. Naveen Prakash Shah
   MBBS, MD, FCCP. Chief of PMDT unit and Senior Consultant Chest Physician at the National TB Control Center (NTCC), Nepal
4. Dr. Lungten Wangchuk
   MBBS, MPH (Major Epidemiology,USA)
   Team lead of Communicable disease unit at WHO country office Nepal
   WHO Fellow for TB Medical Officer, Certificate in Public Health Leadership in Developing Countries, WHO fellow for Advanced Research
5. Dr. Sharad Kumar Sharma
   Ph.D., Chief of Monitoring and Evaluation Section at NTCC

Co-facilitators

6. Dr. Bhabana Shrestha
   National TB expert, Chief – GENETUP/NATA Nepal
7. Dr. Pramod Raj Bhattarai
   DR TB medical officer at Damien Foundation Nepal
8. Mr. Ratna Bhattarai
   MPH, Senior MnE specialist, Save the children/Global Fund program at NTCC.
9. Ms. Meera Hada
   BMLT, Lab focal person, National TB Reference Lab, NTCC

Timing	Description	Facilitators	Remarks
Day 1 (24th June 2020, Wednesday)			
9:00 – 9:15 AM	Welcome address and Message from NTC	Dr. Anuj Bhattachan, Director NTC	
9:15- 9:25 AM	Message from WHO Country Office	Dr. Lungten Wangchuk	
9:25 – 9:35 AM	Message from Chief of PMDT	Dr. Naveen Prakash Shah	
9:35-10:00 AM	Introduction of facilitator and Participants	All participant	
10:00 – 10:20 AM	Pre-test	Asif and others to support	
10:20-10:50 AM	Epidemiology of TB/DR TB in Nepal Q & A (10 Mins)	Dr. Sharad Sharma	
Break (10 mins)			
11:00 – 11:15 AM	Basic Communication Skills to impart Training	Dr. Asif Muhammad	
11:15-12:00 AM	WHO consolidated guidelines on tuberculosis – drug-resistant TB treatment Q & A (10 Mins)	Dr. Vineet Bhatia	
12:00-1:00 PM	Evidence summary for reclassification of drugs Q & A (10 Mins)	Dr. Vineet Bhatia	
1:00- 2:30 PM	Diagnosis of TB/DR TB & Clinical Implications		
	- Global context (45 mins) - Definition used for DR TB practice (15 mins)	Dr. Asif Muhammad	
	- In the context of Nepal (20 mins)	Dr. Naveen Prakash Shah	
	- Q & A (10 Mins)		

Timing	Description	Facilitators	Remarks
Day 2 (25th June 2020, Thrusday)			
10:00-10:40 AM	Laboratory processes in DR TB diagnosis, follow up and management in Nepal Q & A (10 Mins)	Ms. Meera Hada	
10:40 -11:50 AM	Treatment strategies in RR/MDR TB (MDR TB, failures and relapse case of MDR TB) as per new guidelines (Nepal) Q & A (10 Mins)	Dr. Asif Muhammad Dr. Bhawana Shrestha	
Break (10 mins)			
12:0 - 12:40 AM	Treatment with Standardized Shorter MDR TB Regimen Q & A (10 Mins)	Dr. Pramod Raj Bhattarai	
12:40 - 1:50 PM	Treatment of Patients with additional resistance (Pre XDR, XDR TB) Q & A (10 Mins)	Dr. Asif Muhammad	
1:50 - 2:00 PM	Summarize (day 1 and 2)	Dr. Asif Muhammad	

Timing	Description	Facilitators	Remarks
Day 3 (26th June 2020, Friday)			
10:00-10:30 AM	Treatment of Mono & Poly DR TB other than MDR, Pre XDR and XDR TB Q & A (10 Mins)	Dr. Asif Muhammad	Questions and answers
10:30-11:45 PM	aDSM & Causality assessment Q & A (10 Mins)	Dr Lungten	Including Exercise and discussion
Closing by director 15 mins			
Break (10 mins)			
12:10 -1:10 PM	Management of DR TB in special situation (eg. Children, pregnancy, etc) Q & A (10 Mins)	Dr. Asif Muhammad	
1:10-2:10 PM	Identification & Management of major drug side effects (Hepatotoxicity, Anemia, Peripheral neuropathy, Nephrotoxicity, Ototoxicity, cardiotoxicity) Q & A (10 Mins)	Dr. Naveen Prakash Shah	Including case scenarios and exercises
2:10-3:10 PM	Recording, Reporting, and M&E of DR TB	Mr. Ratna Bhattarai Dr. Asif Muhammad	
3:10- 3:20 PM	CLSOING	Director NTCC and facilitators	

List of Participants

	Name	Post	Organization	Email
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