TUBERCULOSIS AND DIABETES MANAGEMENT GUIDELINE

2023



Government of Nepal

Ministry of Health and Population

National Tuberculosis Control Centre

Thimi, Bhaktapur

TABLE OF CONTENTS

_1	INTRODUCTION	1
	1.1 BACKGROUND AND RATIONAL	1
	1.2 GUIDELINE DEVELOPMENT PROCESS	2
	1.3 GOAL AND OBJECTIVES	3
2	AREAS FOR COLLABORATIONS	4
	A. ESTABLISH MECHANISMS FOR COLLABORATION	4
	B. DETECT AND MANAGE TUBERCULOSIS IN PATIENTS WITH DIABETES MELLITUS	4
	C. DETECT AND MANAGE DIABETES IN PATIENTS WITH TUBERCULOSIS	6
3	INDICATORS FOR EVALUATING COLLABORATIVE ACTIVITIES	8
	1. Tuberculosis in patients with diabetes	8
	2. Diabetes in patients with tuberculosis	8
4	IMPLEMENTING COLLABORATIVE ACTIVITIES & EVALUATING THEIR IMPACT	10
	1. Coordination and communication	10
	2. Screening, testing and treatment	10
	3. Capacity building	10
	4. Monitoring and evaluation	10
	5. Innovation and research	10
	6. Logistic Management	10
5	ANNEXURES	11
	Annex-I. ToR-Tuberculosis Technical Working Group (TWG)	11
	Annex-II. Drug Regimen for TB Treatment	12
	Annex-III: Dosage and frequency of the drug regimen	13
	Annex-IV: Special Situations	13
	Annex-V: Adverse effects of the Anti-TB drugs	14
	Annex-VI: Treatment of diabetes	15
	Annex-VII: HMIS 6.1: Presumptive TB Register	16
	Annex-VIII: HMIS 6.4A: TB-Treatment Management Card (HF)	17
	Annex-IX. List of Participants involved in guideline development process	18
	References	20
	Additional Bibliographies	20



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FOREWARD

Diabetes Mellitus (diabetes) and Tuberculosis (TB) have existed for centuries. However, the situation has changed dramatically in the past few decades with the exponential increase in the occurrence of diabetes in Nepal and the association between TB and diabetes. These two factors play a synergetic role in causing human suffering.

Diabetes increases the risk of developing TB. Consequently, rates of TB are higher in people with diabetes than in the general population. Moreover, diabetes can worsen the clinical course of TB, and TB can worsen glycemic control in people with diabetes. People suffering with both conditions thus require careful attention. Strategies are needed to ensure that optimal care is provided to patients with both diseases. TB must be diagnosed early in people with diabetes, and diabetes must be diagnosed early in people with TB. National Tuberculosis Program (NTP) has been recognized as the largest and the fastest expanding TB control program in Nepal. Its goal is to decrease mortality and morbidity due to TB and cut transmission of infection until TB ceases to be a major public health problem in Nepal.

I am confident that this guideline will be instrumental in guiding health care professionals working in TB diagnosis and treatment services, in diabetic /non-communicable disease clinics that included clinicians, nurses, public health workers and program managers where services may be more integrated.

This guideline and their finalization would not have been possible without the consistent technical assistance and support of DEAN, SAFES, SIMON, Nepal Medical Association, Nepalese Respiratory Society. We would also like to acknowledge the special contribution of WHO and Save the Children, who provided their valuable inputs based on their experience on implementing the TB-Diabetes Collaborative activities.

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ABBREVIATIONS

ATT Anti TB Treatment

CME Continuing Medical Education

DEAN Diabetic and Endocrinology Association of Nepal

DM Diabetic Mellitus

DOTS Directly Observed Therapy, Short-course

FBS Fasting Blood Sugar HbA1c Glycated hemoglobin

HIV Human Immunodeficiency Virus

HMIS Health Management Information System IEC Information Education Communication

NCD Non-Communicable Disease

NTCC National Tuberculosis Control Center

NTP National Tuberculosis Program
OGTT Oral Glucose Tolerance Test
OPD Out-patient Department

SAFES South Asian Federation of Endocrine Societies

RR Rifampicin Resistance

TB Tuberculosis

The Union International Union Against Tuberculosis and Lung Disease

TWG Tuberculosis Technical Working Group

WHO World Health Organization

1. INTRODUCTION

1.1. BACKGROUND AND RATIONAL

Diabetes Mellitus (DM) has been associated with a two-to-three-fold risk of tuberculosis (TB) and a twofold risk of death during TB treatment(1), with a stronger association in the presence of other risk factors. The probability of developing TB disease is much higher among people with diabetes. An estimated 371,000 TB cases were attributed to diabetes globally in 2021(2). In addition, DM has been found to adversely affect outcomes for TB contributing to increased deaths, relapse, treatment failure and even adverse drug interactions. Some recent studies have also found association of TB with glucose intolerance, inadequate glycemic control, and hyperglycemia.

The situation in Nepal is also quite similar to the global statistics. Around 3300 TB cases were attributed to diabetes in Nepal in 2021 (2) as shown in **Figure 1**, where prevalence of TB is 416 per 100,000 population and around 69,000 of people developed TB in 2018 (prevalence survey). Moreover, several studies have reported DM as factors associated with poor treatment outcomes among TB patients in Nepal (3–5).

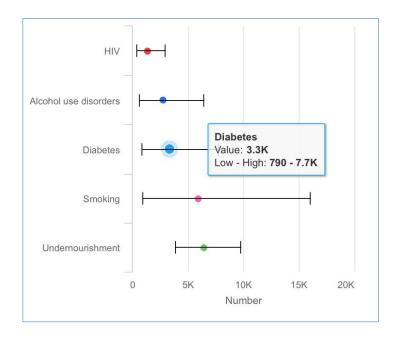


Figure 1

The International Diabetes Federation has estimated the number of people with diabetes to increase by around 50 percent between 2019 and 2045 comprising to increment in TB cases as well. Therefore, with the aforementioned risks of developing TB among diabetic and adverse effects on treatment outcomes for both, there is significant need for collaborative actions on TB and diabetes care. The World Health Organization (WHO) has hence recommended three key collaborative actions for care of people with diabetes and TB in the "Collaborative framework for care and control of TB and Diabetes" based on

which, this "Tuberculosis and Diabetes Management Guideline on-2023" has been developed.

Table 1. Areas outlined in the Collaborative framework for care and control of TB and diabetes)

A. Establish mechanisms for collaboration

- A.1. Set up means of coordinating diabetes and TB activities
- A.2. Conduct surveillance of TB disease prevalence among people with diabetes in medium and high-TB burden settings
- A.3. Conduct surveillance of diabetes prevalence in TB patients in all countries
- A.4. Conduct monitoring and evaluation of collaborative diabetes and TB activities

B. Detect and manage TB in patients with diabetes

- B.1. Intensify detection of TB among people with diabetes
- B.2. Ensure TB infection control in health care settings where diabetes is managed
- B.3. Ensure high-quality TB treatment and management in people with diabetes

C. Detect and manage diabetes in patients with TB

- C.1. Screen TB patients for diabetes
- C.2. Ensure high-quality diabetes management among TB patients

1.2. GUIDELINE DEVELOPMENT PROCESS

In September 2022, NTCC, SAFES and DEAN organized a meeting, to initiate TB screening among diabetic mellitus and identify priority questions for systematic reviews of the links between diabetes and TB. The meeting prioritized discussion to be addressed on (1) To ensure early diagnosis of DM among people with TB and the diagnosis of TB among people with DM. (2) To improve treatment outcomes of both diseases through initiating TB treatment and DM treatment for persons with both diseases. (3) Develop a guideline and tools for management of tuberculosis -diabetes mellitus. Subsequently, in May 2023, The National Tuberculosis Control Center (NTCC) along with NTP partners, public and private sector clinicians developed a draft framework for the guideline on the management of Tuberculosis and Diabetes Mellitus. The country identified a need for the guideline on the co-management of the two diseases after various discussions and meetings with NTCC, partners and diabetologists and endocrinologist. The draft guideline is then subjected to external review by relevant stakeholders, including healthcare providers, professional associations, and patient's advocacy groups to ensure a comprehensive and inclusive perspective. The feedback received is carefully considered and the guideline is revised accordingly.



1.3. GOAL AND OBJECTIVES

Goal

The overall goal of the "Tuberculosis and Diabetes Management Guideline-2023" is to reduce TB and diabetes co-morbidity and mortality in Nepal.

Objectives

- To improve early detection and management of tuberculosis in patients with diabetes.
- To improve early detection and management of diabetes in patients with tuberculosis.
- To strengthen cross referral mechanisms for tuberculosis and diabetes management.
- To strengthen surveillance mechanism for TB and diabetes.

2. AREA OF COLLABORATIVE ACTIONS

A. ESTABLISH MECHANISMS FOR COLLABORATION

The existing Technical Working Group (TWG) for Tuberculosis will provide oversight for the implementation of TB and Diabetes related activities in the country. The ToR of TWG is attached in ANNEX-I. Thematic specialists will be invited to TWG meetings for technical inputs into the program.

B. DETECT AND MANAGE TUBERCULOSIS IN PATIENTS WITH DIABETES MELLITUS

Detecting and managing TB in patients with Diabetes included two key interventions below:

- i. Screening people with Diabetes for TB
 TB screening should be done with chest X-ray
 - At the time of diabetes mellitus diagnosis
 - During follow up visits if there is onset of symptoms and/or history of contact with TB or when have sudden increase of medication for diabetes mellitus (If chest X-ray is suggestive of TB, take appropriate samples for TB testing. Figure-2)
- ii. Treatment of TB in people with Diabetes
 - Treatment should be started as per the national guidelines on TB management.
 - Ensure TB medicines should be administered and monitored until successful completion of treatment.
 - Measure Glycemic Control, FBS (Fasting Blood Sugar), 2 Hr PP, if accessible perform the glycated Hemoglobin (HbA1c) test
- iii. Refer patients to nearest DOTs center for treatment.
- iv. TB patients who require steroids (TB meningitis, TB pericarditis, TB adrenalitis, TB myelitis) control of blood sugar should be assessed by doing FBS, PPBS & HbA1c. Consultation with endocrinologist / general physician should be done before and after initiation of steroid.

Person with DM Is person already on treatment of TB Yes No Continue management If, (1) Onset of of DM-TB and monitor symptom* and/or adherence & response history of contacts with TB, (2) Sudden increase of DM medication If NO If YES to any of above (1) Take appropriate sample (sputum, (1) Provide education on TB Pleural fluid, Lymphnode aspirate, CSF (2) Continue management of DM and passive TB screening in subsequent visit etc. for Xpert or microscopy) (2) Conduct chest X-ray or refer to TB (3) Conduct Chest X-ray annually If X-ray suggestive of TB, take sputum sample for Xpert or microscopy No diagnosis of active TB Active TB diagnosed Treat appropriately for TB at the TB Consider further evaluation if clinic. Treat as per NTP guideline required; continue DM care

Figure-2: Algorithm for the screening people with diabetes for Tuberculosis

^{*} Onset of symptom: (1) Cough of any duration, (2) Fever, (3) unexplained weight loss, (4) night sweats, (5) any symptoms suggestive of EP TB

C. DETECT AND MANAGE DIABETES INPATIENTS WITH TUBERCULOSIS

Early detection and management of diabetes in TB patients is crucial to improve treatment outcomes and reduce complications. DOTS clinics are strongly encouraged to test all newly enrolled TB patients for Diabetes as per availability of resources and facilities.

1. Screening Criteria:

All TB patients should undergo screening for Diabetes, regardless of age or TB type (pulmonary or extrapulmonary).

2. Screening Methods:

a. Random Blood Sugar Test (RBS): Random blood sugar is the preferred screening method at the time of patient visit at health facility. Random blood sugar level ≥ 200 mg/dL (11.1 mmol/L) indicates a diagnosis of DM in presence of symptoms. If asymptomatic people repeat the test to confirm DM.

b. Fasting Blood Sugar (FBS) and 2 Hrs post prandial (PP) Blood Sugar Test:

- FBG level > 126 mg/dl (7.0 mmol/l) indicates a diagnosis of Diabetes.
- 2 hrs. PP blood sugar ≥ 200 mg/dl (11.1 mmol/l) indicates a diagnosis of Diabetes.

c. Glycated Hemoglobin (HbA1c) test:

HbA1c level > 6.5% (48 mmol/l) indicates a diagnosis of Diabetes. Consider using HbA1c test depending on availability of test facilities if FBG and 2 hrs. PP blood sugar are inconclusive [FBG 110-125 mg/dl (6.1-6.9 mmol/l) or 2 hrs. PP blood sugar 126-200 mg/dl (7-11.1 mmol/l)].

d. Osmotic Symptom

Osmotic Symptom like (1) feeling tense, irritability, restlessness, poor concentration (agitation) (2) thirst, dry mouth, need to urinate, not feeling right, sweet/funny taste, weakness (osmotic) (3) dizziness, blurred vision, light-headedness, weakness (neurological) (4) headache, nausea (malaise) is an optional screening method at the time of patients visits to health facilities.

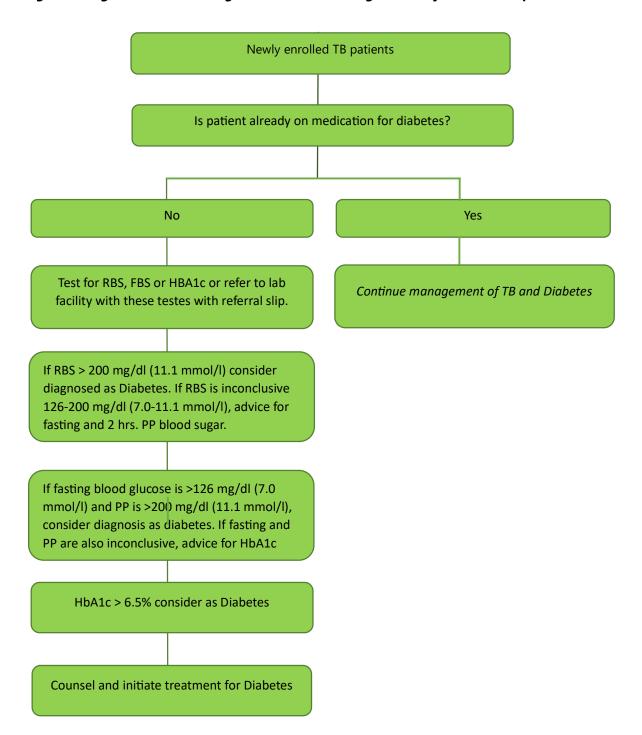
3. Screening Process:

a. Perform screening for DM at the time of TB diagnosis or during the early phase of TB treatment. b. Healthcare providers should educate patients about the importance of screening for Diabetes and the benefits of early diagnosis.

4. Management and Follow-up:

- a. If a patient is diagnosed with Diabetes, manage according to the treatment protocol or refer to a higher center with DM management facility within 15 days for treatment.
- b. If the initial screening results are normal, repeat screening in following conditions.
 - i. Sputum non converters
 - ii. Clinically deteriorated patients
 - iii. Treatment Failure Cases

Figure-3: Algorithm for the diagnosis diabetes among the newly enrolled TB patients.



Note: If the initial screening results are normal, re-screen for non-converter and clinically deteriorated patients.

3. INDICATORS FOR EVALUATING COLLABORATIVE ACTIVITIES

By monitoring a specific set of essential process and outcome indicators, all care providers can effectively collaborate and strive towards shared objectives. This approach would facilitate the swift implementation of collaborative activities at the country level. The following indicators are suggested for monitoring at various levels, such as clinics, palikas, districts, provinces, or nationally. The selection of these indicators, as well as the potential inclusion of additional ones, should be based on the local context and the scope of collaborative efforts addressing TB and diabetes.

Table 2: Indicators to Track TB and Diabetes Collaboration.

Indicators	Numerator	Denominator	Source
1.	Tuberculosis in pa	tients with diabetes	
Proportion of persons diagnosed with Diabetes	Total New Patients diagnosed as Diabetes	Total New OPD visits	OPD Register HMIS 1.3
Number and proportion of people screened for TB among diabetes	Total cases screened for TB among Diabetes	Total cases registered as Diabetes	HMIS 6.1: Presumptive TB Register
Number and proportion of people Tested for TB among diabetes screened for TB (radiography, sputum smear microscopy, culture, etc).	Total Cases tested for TB in Different Setting (radiography, sputum smear microscopy, culture, etc)	Total cases screened for TB among Diabetes	HMIS 6.1: Presumptive TB Register
Number and Proportion of people diagnosed with TB among Tested.	Total Diagnosed TB Cases	Total Cases tested for TB among Diabetes	HMIS 6.1: Presumptive TB Register
Number and Proportion of people Enrolled in TB treatment among diagnosed.	Total TB Cases Enrolled in TB treatment	Total Diagnosed cases with TB	HMIS 6.1: Presumptive TB Register
2.	. Diabetes in patien	ts with tuberculosis	
Number of TB Cases Eligible for Diabetes Test	Total Number of TB Cases Registered for TB treatment	NA	HMIS 6.4A: TB- Treatment Management Card (HF)
Number and proportion of people Tested for diabetes among TB	Total cases Tested for Diabetes among TB	Total cases registered as TB	HMIS 6.4A: TB- Treatment Management Card (HF)

Indicators	Numerator	Denominator	Source
Number and Proportion of people diagnosed with Diabetes among Tested.	Total Diagnosed Diabetes Cases	Total Cases tested for Diabetes among TB	HMIS 6.4A: TB- Treatment Management Card (HF)
Number and Proportion of people Enrolled in DM treatment among diagnosed.	Total Diabetes Enrolled in DM treatment	Total Diagnosed cases with Diabetes	HMIS 6.4A: TB- Treatment Management Card (HF)
TB treatment outcomes among people with diabetes.	Outcome given (Cured, Completed, Failed, Died, Loss to Follow-up, treatment success, Not- Evaluated)	Total TB Diabetes cases Registered during the period.	HMIS 6.4A: TB- Treatment Management Card (HF)

^{*} All the sites (Public and Private HFs) should use the "HMIS 6.1: Presumptive TB Register" for screening and Testing.

4. IMPLEMENTING COLLABORATIVE ACTIVITIES & EVALUATING THEIR IMPACT

1. Coordination and Communication

- Collaborate with educational institution to incorporate TB and DM management in the curriculum.
- Awareness raising activities including development and dissemination TB diabetes related IEC material.
- Continue Medical Education (CME) on TB-Diabetes at diabetes clinics and with stakeholders (administrators, partners etc.) at local level.

2. Screening, testing and treatment

- Establishing service delivery protocols that address joint activities to improve diagnosis and management of diabetes among TB patients:
 - Screening of all registered TB patients for diabetes
 - Ensuring diabetes management among TB patients
- Establishing service delivery protocols that address joint activities to improve diagnosis and management of TB among diabetic patients:
 - Intensified detection of active TB disease among diabetes patients
 - Ensuring TB treatment and management in diabetes patients
- Integrate bi-directional screening in diabetic and TB clinics
- Establish mechanism for cross-referral mechanism for the testing and treatment management.

3. Capacity building

- Include TB diabetes session in regular TB modular training
- Continuing Medical Education (CME) with TB-Diabetes session for clinicians and health professionals.

4. Monitoring and Evaluation

- Conduct joint M&E visit with member of Diabetic Association at least 2 times in a year at TB diabetic collaborative clinic
- Conduct annual program review workshop of TB and DM collaboration

5. Innovation and Research

- Conduct at least one operational research on TB and DM co-morbidity
- Provide support for research in TB and DM co-morbidity with academic institution

6. Logistics Management

- Ensure regular supply of commodities related to sputum collection & transportation and consumables for TB diagnosis.

5. ANNEXURES

Annex I. ToR-Tuberculosis Technical Working Group (TWG)

- Support to established governance arrangements and management structure for the program through the meaningful involvement of technical experts, development partners, other stakeholders and civil societies into the process of technical advice, coordination and resource mobilization;
- b. Provide a forum for technical discussion and advice in overall TB program approaches including in the areas of TB care and prevention, TB/HIV collaborative approaches, PPM, DRTB, CSS, etc. inline with the National TB Strategy Plan for Nepal (2016-2021)
- c. Promote understanding and support for the Program targets among technical institutions, professional associations and bilateral/multisectoral and other relevant agencies/partners;
- d. Ensure broad agreement of all relevant stakeholders and key experts regarding the structure and content of the relevant programmatic directions;
- e. Ensure availability of key local and international technical expertise during the development of the initial request for any funding and resource mobilization for TB Programs from different doners
- f. Ensure stakeholder/s contribution and harmonized and are aligned with the National Strategy Plan for TB Control in Nepal 2016-2021
- g. Ensure quality program planning, implementations and monitoring is in line with the NSP for TB control in Nepal
- h. To advise on operational research, implementation lessons and other research evidence from both local and international contexts and ensure that it is used to inform decision-making, revision of policies and inform program planning and implementation where appropriate
- i. To provide oversight and coordination of all different funding sources for TB programme, grants and projects related to TB service delivery;
- j. To provide high quality technical advise and technical sign-off on any proposal, operational research, pilot and other related activities for health related to TB service delivery.
- k. Make technical recommendations that will help to strengthen national efforts to implement policies and strategy for TB control, including M/XDR-TB and TB/HIV coinfection in line with health systems strengthening, and help to monitor progress through set targets in line with the NSP (2016-2021)
- Facilitate the governmental and non-governmental partnership to share up-to-date information, to collectively trouble-shoot problem areas and to discuss possibly contentious issues
- m. Provide technically sound and relevant programmatic direction in a coordinated manner and to provide support to the NTCC in its efforts to provide access to high quality TB services in the country

Annex II. Drug Regimen for T B Treatment

Table 3: Categories of Treatment and their Anti-TB Drug Regimens

TYPE OF TB		INTENSIVE PHASE	CONTINUATION PHASE
New TB cases - Adult and Childhood - Bacteriological or clinically diagnosed - Pulmonary or extra-pulmonary		2HRZE	4HR
Complicated/Severe EP cases (CNS TB, TB Pericarditis, Musculoskeletal TB, Miliary TB etc.)	keletal TB, Miliary TB etc.)	2HRZE	7-10 HRE *
Retreatment cases All forms:	Xpert MTB/RIF— Rifampicin sensitive LPA – Isoniazid sensitive	2HRZE	4HR
1st Rapid DST with Xpert MTB/RIF testing should be done to see the status of resistance to Rifampicin	Xpert MTB/Rif– Rifampicin sensitive LPA – Isoniazid Resistant and FQ sensitive	6 (H)RZE + Levofloxacin (Full Duration)	cin (Full Duration)
Followed by LPA among those having MTB+ve and Rifampicin sensitive for Isoniazid (INH) resistance status.	Xpert MTB/Rif—Rifampicin sensitive LPA — Isoniazid Not known because of no access to LPA	6 HRZE (Full duration)	(1
	Rifampicin sensitive INH resistance and FQ resistant**	6(H)RZE	
DRTB	Refer to national guidlines on DR-TB management (2019)		

^{*} For complicated EP cases, if treatment is required beyond 12 months, then refer to a higher level centre for treatment decisions

^{**}Depending on the patients' response and laboratory evidence, clinicians at the higher-level centre can use laboratory evidence/result to inform futher management where necessary.

Annex-III: Dosage and frequency of the drug regimen

Blister packs are currently used for treatment of TB in Nepal. A single blister pack contains 28 tablets. The number of tablets to give to each patient is based on their weight band and the number of blister packs to be given depends on the number of tablets each patient takes, and the number of days supplied. The following table shows the recommended number of tablets to be given to TB patients in the different weight ranges and the number of blister packs needed for the full course of treatment and numbers to supply using 28-tablet blister packs.

Table 4: TB TREATMENT

Wainbt banda	Intensive Phase	Continuation Phase	INH Resistant (Hr-TB) HRZE Levofloxacin (Lf: 75/150/400/275 250mg	
Weight bands	HRZE 75/150/400/275	HR 75/150		
30-39 kg	2 Tablets	2 Tablets	2 Tablets	2 Tablets
40-54 kg	3 Tablets	3 Tablets	3 Tablets	3 Tablets
55-70 kg	4 Tablets	4 Tablets	4 Tablets	4 Tablets
>70 kg	5 Tablets	5 Tablets	5 Tablets	5 Tablets

Annex-IV: Special Situations

Table 5: Recommendations for special situations when deciding TB treatment.

Special Situation	Recommended regimen
Pregnancy	A pregnant woman should be advised that successful treatment of TB with the standard regimen is important for successful outcome of pregnancy. The first line anti-TB drugs are safe for use in pregnancy.
Breast feeding	Mother should be given normal full course of TB treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to the baby. Mother and baby should stay together, and the baby should continue to breastfeed. Use mask while breast-feeding and practice other infection measures. After active TB in the baby is ruled out, the baby should be given 3 months RH preventive therapy, followed by BCG vaccination.
	Pyridoxine 10 mg daily supplementation is recommended for all pregnant or breastfeeding women taking isoniazid (INH) throughout the TB treatment
TB/HIV	Same regimen as a non-HIV TB patient for same duration.
Oral contraceptive pills	Since rifampicin reduces the effectiveness of oral contraceptives, women should be advised to choose between one of two options for contraception. Following consultation with a clinician, the patient may use an oral contraceptive pill containing a higher dose of estrogen (50 µg); alternatively, some non-hormonal methods of

	contraception may be used throughout rifampicin treatment and for at least one month subsequently
Liver disorder	Patients with hepatitis virus carriage, a past history of acute hepatitis and current excessive alcohol consumption provided that there is no clinical evidence of chronic liver disease can receive usual regimen but should be closely monitored. Exception and an alternate regimen are given below
Renal failure and severe renal insufficiency	The recommended initial TB treatment regimen for patients with renal failure or severe renal insufficiency is same as normal TB treatment. Exception and an alternate regimen are given below:

Annex-V: Adverse effects of the Anti-TB drugs

Minor side effects can be managed at the health facilities. However, if major side effects occur treatment should be stopped, and the patient should be referred to a trained clinician or hospital.

Table 6: COMMON ADVERSE EFFECT OF ANTI-TB DRUGS

SIDE EFFECTS	DRUGS RESPONSIBLE	MANAGEMENT
MINOR ADVERSE EFFECTS		
Anorexia, nausea, vomiting, Abdominal pain (and no jaundice)	Pyrazinamide, Rifampicin	Take drugs with food or juice or before sleeping and reassurance.
Joint pain	Pyrazinamide	Aspirin / Indomethacin
Burning sensation in the feet, tingling	Isoniazid	Pyridoxine 100 mg daily (when better reduce to 25 mg/day
Confusion, sleep disturbance	Isoniazid	Pyridoxine 25 mg/day
Orange/red urine	Rifampicin	Reassurance
Itching, rash without blisters	Any drug (or skin disease)	Phenergan, promethazine
MAJOR ADVERSE EFFECTS		
Deafness	Injectables	Stop Injectables
Dizziness, vertigo, nystagmus	Injectables	Stop Injectables
Jaundice (other causes excluded), hepatitis	All drugs but commonly isoniazid. Also, rifampicin and Pyrazinamide	Stop anti-TB drugs, start the same regimen after two weeks or refer.
Confusion	Most anti-TB drugs	Stop anti-TB drugs, refer
Difficulty with vision	Ethambutol	Stop ethambutol, refer
Shock, purpura, acute renal failure	Rifampicin	Stop rifampicin, refer

Annex-VI: Treatment of diabetes

Metformin is the first-line drug of choice for treating persons with Diabetes 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.

The basic essentials of these three drugs are shown in Table XX

Table 7: Common glucose-lowering drugs used for managing Diabetes Mellitus in TB patients

CHARACTERISTIC	METFORMIN	SULPHONYLUREA DERI- VATES	INSULIN
Drug of choice	First choice	Add-on Used in case there is a contraindication or intolerance to metformin	Use if targets for HbA1c or FBS cannot be reached or if there is symptomatic hyperglycemia
Risk of hypoglycemia	No	Yes	Yes
Starting dose (od = once a day; bid = twice a day)	500 mg od or bid, titrated to a maximum dose of 2000 mg daily	Gliclazide: 40-80 mg OD Glibenclamide: 2.5-5 mg OD Glimepiride: 1-2 mg OD Glipizide: 5 mg OD	10 units basal insulin per day as the starting point
Interaction with rifampicin	Not clinically relevant	Yes, 30-80% lower efficacy with rifampicin	None
Main side effects	Gastrointestinal Lactic acidosis	Hypoglycemia	Hypoglycemia
Use in reduced kidney function (GFR = glomerular filtration rate)	Dose adjustment if eGFR <45 ml/min Contraindication if eGFR <30 ml/min*	Increased risk of hypogly- cemia Preference gliclazide	Can be safely used
Cardiovascular events	Recognized benefit	Neutral	Neutral

^{*}eGFR = estimated glomerular filtration rate.

if measurement of eGFR cannot be done, metformin should not be given to patients with known chronic kidney disease without approval from their treating physician.

People with Diabetes and a history of previous cardiovascular disease should be offered low-dose aspirin and a statin.

People with Diabetes and TB need to be counselled about appropriate lifestyle management (smoking cessation, good diet, and physical activity).

Linagliptin is equally safe, effective, and convenient as Metformin to treat type 2 diabetes that can also be prescribed from middle level healthcare provider, however people with diabetes need to be refer to the healthcare center for the further treatment by giving medicine for a maximum of 2 weeks, and before starting Linagliptin, LFT and RFT test are suggested.

Annex-VII: HMIS 6.1: Presumptive TB Register

		नेपाल सरकार	
		स्वास्थ्य व्यवस्थापन सूचना प्रणात्री	
		सम्भावित क्षयरोग दर्ता रजिष्टर	
		PRESUMPTIVE TUBERCULOSIS REGISTER	
न्वास्थ्य संस्थाको नार	R:		
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Annex-VIII: HMIS 6.4A: TB-Treatment Management Card (HF)

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Annex IX. List of Participants involved in guideline development process

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- 7. Dr Bhagwan Maharjan, TB Lab Specialist, SCI-GF
- 8. Dr Bhawana Shrestha, Project Manager, NATA
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- 10. Dr Buddha Karki, Endocrinologist
- 11. Dr CP Acharya, Chest Physician, Manipal Teaching Hospital
- 12. Dr Deena Shrestha, Endocrinologist
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- 16. Dr Gokul Mishra
- 17. Dr Jasmine Tuladhar, Endocrinologist
- 18. Dr Jyoti Bhattarai, Endocrinologist
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- 23. Dr Mimi Giri, Endocrinologist
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