Diagnosis and Management of Tuberculosis

Chapter 3

Tuberculosis Treatment and Management

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Abbreviations

AFB: Acid-fast Bacilli; ART: Anti -Retroviral Therapy; CTC: Care and Treatment Centre; DOT: Direct Observed Treatment; DST: Drug Susceptibility Test; EPTB: Extra- Pulmonary Tuberculosis; HIV: Human Immunodeficiency Virus; M. TB: Mycobacterium Tuberculosis; MDR-TB: Multi-drug Resistance Tuberculosis; NTPs: National TB Programs; PAS: Para-Aminosalicyclic Acid; PCT: Patient Centred TB Treatment; PTB : Pulmonary Tuberculosis; TB: Tuberculosis; WHO: World Health Organization; XDR-TB: Extreme Drug Resistance Tuberculosis

1. Introduction

1.1 Chapter objectives

This chapter has four main sections; introduction, TB treatment, management and challenges: The introduction section defines what is tuberculosis (TB) and how it is spread, risk factors, highlights on the historical perspective of TB including; its discovery and treatment (discovery of drugs). The section also explains on the types of TB and burden of TB globally. The treatment section describes the importance of TB treatment, treatment duration and phases, categories of patients, current treatment regimen for adult and for children. The management section gives details on different approaches used in the management of TB patients with main focus on involvement of communities. The section on challenges highlights challenges in TB treatment, management, TB/HIV co-infection, programmatic challenges and in special situations such as MDR-TB and prisons.

1.2 What is tuberculosis?

Tuberculosis is a chronic infectious disease mainly caused by *Mycobacterium tuberculosis (M. TB)* and occasionally by *Mycobacterium bovis* or *Mycobacterium africanum*. The disease is spread through air (an air born disease). Transmission from one person to another occurs through inhalation of droplets during coughing, laughing, talking, sneezing and singing. However, the most common means of transmission is through coughing. The potential sources of infection are untreated smear-positive patients who are in the community.

1.3 Risk factors contributing to infection and development of disease

An individual's risk of infection depends on several factors, including;

- Concentration and size of infectious droplets,
- Extent or duration of exposure,
- Prevalence of TB in the community; (the higher the prevalence of TB in the community, the higher the risk of exposure and infection).
- Overcrowding and prolonged stay with an infectious person in a poorly ventilated and lighted environment, and
- Individual's immune status and susceptibility to infection.
- Malnutrition and other conditions such smoking, diabetes (Daniel, et al., 2011).

The risk of progression from infection to active disease depends on the status of the individual's immune system. It is well documented that 90% of people without human immunodeficiency virus (HIV) infection who are infected with *M.tuberculosis* do not develop TB disease. Tuberculosis and HIV co-infected people have annual risk of 5-10%,and20-30 times higher risk of developing TB disease during their life time than people without HIV infection (NTLP Manual 2013).

1.4 Historical perspective of Tuberculosis

Tuberculosis has been known to mankind since ancient times. Historically, earlier TB disease has been called by numerous names including; Consumption (because of the severe weight loss and to "consume" the patient); Phthisis pulmonaris and the White plague (because of the extreme pallor seen among those infected). Consumption, phthisis, scrofula, Pott's disease, and the White Plague are all terms used to refer to tuberculosis throughout history. It is generally accepted that the microorganism originated from other, more primitive organisms of the same genus Mycobacterium. Even today after the development of advanced screening, diagnostic and treatment methods for the disease, a third of the world's population has been exposed and is infected with the organism. In the 19th century, TB was known as **"the captain of all men of death".** It is still true to a large extent today.

Tuberculosis in Ancient times: The organism causing tuberculosis – M. TB existed since 15,000 to 20,000 years ago. It has been found in relics from ancient Egypt, India, and China. Among Egyptian mummies spinal TB, known as Pott's disease has been detected by archaeologists.

Tuberculosis in the middle ages: Evidence of TB of the cervical lymph nodes or lymph nodes of the neck termed **scrofula** was found in the middle ages. It was termed as the **"king's evil"** and was widely believed that the kings of England and France could cure scrofula simply by touching those affected.

Tuberculosis in the 18th century: In the 18th century in Western Europe, TB reached its peak with a prevalence as high as 900 deaths per 100,000 population. Poorly ventilated and overcrowded housing, primitive sanitation, malnutrition and other risk factors led to the rise. In deed the term White plague emerged around this time. During this period, famous men and women over ages suffered from this disease. Notable among these were poets John Keats and Percy Bysshe Shelley, the authors Robert Louis Stevenson, Emily Bronte, and Edgar Allen Poe, the musicians Nicolo Paganini and Frederic Chopin to name a few.

Discoveries pertinent to tuberculosis: The tubercle bacilli or the causative organism of tuberculosis was demonstrated by Robert Koch in 1882. Robert showed that the organism's unique protein coat made it difficult to visualize earlier until a specific stain called the ZeihlNeelson stain was discovered. After this discovery, the bacteria was called Koch's bacillus and since it took up the red acidic dye, it was called acid fast bacilli (AFB). Koch was awarded the Nobel Prize in 1905. In 1895 Wilhelm Roentgen developed X-rays which further advanced diagnostics of tuberculosis. Discovery of X-ray allowed early diagnosis and isolation of infected individuals.

Isolation: In the 19th century the concept of keeping TB patients isolated in a sanatorium started. It was initially started in Silelsia in 1859 by Hermann Brehmer.In 1884, Edward Livingston Trudeau started the first sanatorium in the United States. From that time, infectious persons were isolated from society and treated with rest and improved nutrition.

Development of vaccine for TB: In the 1880s Louis Pasteur began the concept of development of vaccines against anthrax, chicken cholera, and, later, rabies. In 1908, the French scientists **Albert Calmette and Camille Guerin** grew Koch's bacillus in several mediums to decrease their virulence and increase the capacity to produce immunity. This led to the now famous vaccine called BCG named after the two founders. BCG was introduced in 1921.

Surgery for TB: Before antibiotics were found effective against TB, surgical treatment of TB was common and often lifesaving. Dr. James Carson, a Scottish physician (1821), began treatment by draining pleural effusion from around the lungs and found surgery helped prolong life. Various techniques evolved but due to lack of efficacy faded away after advent of anti-

tubercular drugs.

Anti-tubercular drugs: In 1944 -antibiotics were used against TB for the 1st time after the discovery of streptomycin. Use of this agent alone led to antibiotic resistance that is still a major problem.Better results followed the development of para-aminosalicyclic acid (PAS). Unlike streptomycin, PAS was an oral agent. In 1950's - More effective drugs like isoniazid (INH) came in and treatment with rifampicin followed. Currently, there are about 20 agents with activity against mycobacterium.

1.5 Types of tuberculosis disease

There are two main types of TB: pulmonary and extra-pulmonary. The most common form is pulmonary tuberculosis (PTB), which accounts for 80% of all cases of TB. Pulmonary TB is the infectious form and affects the lungs. Extra-pulmonary tuberculosis (EPTB) affects organs other than the lungs (e.g., pleura, lymphnodes, abdomen, genitourinary tract, skin, joints and bones, meninges); it is usually non-infectious and accounts for 20% of all cases of TB (NTLP Manual 2013).

1.6 Burden of Tuberculosis

Tuberculosis is a major public health problem throughout the world. About a third of the world's population is estimated to be infected with the tubercle bacilli and is at risk of developing active disease. According toWHO, in 2016 there were 6.3 million new cases of TB globally, equivalent to 61% of the estimated incidence of 10.4 million. TB is the ninth leading cause of death worldwide and the leading cause from a single infectious agent, ranking above HIV/AIDS. In 2016, there were an estimated 1.3 million TB deaths among HIV-negative people and an additional of 374 000 deaths among HIV-positive people. An estimated 10.4 million people fell ill with TB in 2016: 90% were adults, 65% were male, 10% were people living with HIV (74% in Africa) and 56% were in five countries; India, Indonesia, China, the Philippines and Pakistan. Furthermore, drug-resistant TB is continuing to be a threat, for instance in 2016, there were 600 000 new cases with resistance to rifampicin (RRTB), the most effective first-line drug, of which 490 000 had multidrug-resistant TB (MDR-TB). Almost half (47%) of these cases were in India, China and the Russian Federation (WHO report 2017).

1.7 HIV infection and multi-drug resistance TB

The most important recent changes in the history of TB have been the impact of the HIV epidemic and the emergence of resistance to anti-TB drugs. HIV infection exacerbates the TB epidemic through its impact on susceptibility *M. tuberculosis* infection and progression from infection to active disease. HIV infection increases the rate at which *M. tuberculosis* infections are acquired and increases the likelihood that people who are already infected will

develop active TB disease (WHO 2008). The impact of HIV has been greatest in countries of southern and eastern Africa, where up to 40% of adults may be infected with HIV and where the incidence of TB has increased 4–5-fold within 10 years. Infection with both *M. tuberculosis* and HIV is prevalent in some population groups in certain countries of South-East Asia, including Cambodia, China, India, Thailand and Viet Nam. The development and increasing importance of anti-TB drug resistance are of concern to TB control programs because drug-resistant TB is much more difficult to manage and more expensive to treat than fully drug-susceptible TB.

Section Two: Treatment

2. Tuberculosis Treatment

Treatment for TB is usually initiated once the diagnosis is confirmed. An effective TB treatment is of the paramount importance in TB care and control, since it terminates the transmission chain and eventually leads to a reduction of the disease burden in the community. The effectiveness of TB treatment depends on the use of the right anti-TB drug combinations both in the intensive and the continuation phases, prescribed and taken in the correct doses according to the schedule and for the required length of time.

2.1 Treatment phases and duration

There two phases of TB treatment; initial or intensive and continuation. Treatment of TB usually takes 6-8 months depending on weather the patient is newly diagnosed or previously treated case. Newly diagnosed are treated for six months while previously are treated for eight months (**Table 1**).

Patient category	Treatment phases and Duration		Total treatment duration
	Intensive	Continuation	
Newly diagnosed	2 months	4 months	6- months
Previously treated (Re-treatment)	3 months	5 months	8- months

Table 1:Treatment phases and duration by patient category

2.2 Aim of TB treatment

Specifically, treatment of TB aims to:

- 1. Cure the patient and restore quality of life and productivity.
- 2. Prevent relapse of TB.
- 3. Reduce transmission of TB to others.
- 4. Prevent the development and transmission of drug-resistant tubercle bacilli.

5. Prevent death from active TB or its late effects.

2.3 Definition of TB case classifications

Tuberculosis cases are classified according to anatomical sites and other conditions to facilitate recording and reporting and to identify the most infectious patients for infection control. The classifications include the following:

- a) Anatomical site of disease
- b) History of previous treatment
- c) Drug resistance
- d) HIV status

a) Classification based on anatomical site of disease

This classification is based on the site of the infection; pulmonary or extra pulmonary.

Pulmonary tuberculosis (PTB): Refers to a case of TB involving the lung parenchyma. Miliary TB is classified as PTB because there are lesions in the lungs. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitutes a case of EPTB. A patient with both pulmonary and extra-pulmonary tuberculosis is classified as a case of PTB.

Extra-pulmonary tuberculosis (EPTB): Refers to a case of TB involving organs other than the lungs (e.g., pleura, lymphnodes, abdomen, genitourinary tract, skin, joints and bones, meninges). EPTB cases can be either bacteriologically confirmed or clinically diagnosed. Identification of *M. tuberculosis* (as opposed to histology) should be the basis of bacteriological confirmation of EPTB. The case definition of an EPTB case with several sites affected depends on the site representing the most severe form of the disease.

b) Classification based on history of previous TB treatment (patient registration group)

This classification focuses on history of previous treatment only and is independent of bacteriological confirmation or site of disease (**Table 2**).

	Patient categories	Description of the category	
1	New patient	Has never had treatment for TB, or has taken anti-TB drugs for less than one month.	
2	Previously treated patient	Has received one month or more of anti-TB drugs in the past.	

Table 2: Classification of patients based on history of previous TB treatment

	Patient categories	Description of the category	
3	Relapse patient	Has been previously treated for TB, was declared cured or treatment completed at the end of the most recent treatment episode, and is now diagnosed with a recurrent episode of TB (either a true relapse or a new episode of TB caused by re-infection).	
4	Treatment after failure patient	A patient who was previously treated for TB and whose treatment failed at the end of the most recent treatment episode.	
5	Treatment after loss to follow-up patient	A patient previously treated for TB who was declared lost tofollow-up at the end of the most recent treatment episode (previously known as "return after default").	
6	Other previously treated patientA patient who was previously treated for TB but with an unknown of undocumented outcome for the most recent treatment episode (previously as "others").A patient with an unknown previous TB treatment history does not fit into the categories listed above.		

c) Classification based on drug – resistance

Drug-resistant patients are defined as those with tubercle bacilli that are resistant to both rifampicin and isoniazid (MDR-TB). Patients with MDR-TB whose tubercle bacilli have additional resistance to a second-line injectable (capreomycin, kanamycin, or amikacin) and a fluoroquinolone (ofloxacin, moxifloxacin, levofloxacin, or gatifloxacin) are classified as extreme drug resistance TB patients (XDR-TB).

There are about five categories of drug-resistance classification based on drug susceptibility test (DST) results:

- Monoresistance: Resistance to one first-line anti-TB drug only.
- **Polydrug resistance:** Resistance to more than one first-line anti-TB drug, other than both isoniazid and rifampicin.
- Multidrug resistance (MDR TB): Resistance to at least both isoniazid and rifampicin.
- Extensive drug resistance (extensively drug-resistant tuberculosis, or XDR TB): Resistance to any fluoroquinolone and at least one of three second-line injectable drugs (capreomycin, kanamycin, and amikacin), in addition to multidrug resistance.
- **Rifampicin resistance:** Resistance to rifampicin detected using culture or molecular tests (phenotypic or genotypic methods), with or without resistance to other anti-TB drugs. This includes any resistance to rifampicin, in the form of monoresistance, multidrug resistance, polydrug resistance, or extensive drug resistance.

d) Classification based on HIV status

HIV-positive TB patient: A patient with TB (bacteriologically confirmed or clinically diagnosed) who has a documented HIV-positive result, such as a CTC1 card, or is registered in an HIV Care and Treatment Centre (CTC), or has a positive HIV result from testing conducted at the time of TB diagnosis.

HIV-negative TB patient: A patient with TB (bacteriologically confirmed or clinically diagnosed) who has a documented negative HIV result from a test conducted at the time of TB diagnosis. HIV-negative TB patients subsequently found to be HIV positive should be reclassified as HIV-positive TB patients.

2.4 HIV and multi-drug resistance TB

The most important recent changes in the natural history of TB have been the impact of the HIV epidemic and the emergence of resistance to anti-TB drugs.HIV infection exacerbates the TB epidemic through its impact on susceptibility to *M. tuberculosis* infection and progression from infection to active disease.

HIV infection increases the rate at which *M. tuberculosis* infections are acquired and increases the likelihood that people who are already infected will develop active TB disease. The impact of HIV has been greatest in countries of southern and eastern Africa, where up to 40% of adults may be infected with HIV and where the incidence of TB has increased 4–5-fold within 10 years. Infection with both *M. tuberculosis* and HIV is prevalent in some population groups in certain countries of South-East Asia, including Cambodia, China, India, Thailand and Viet Nam (WHO 2008).

The development and increase of MDR-TB pose a great challenge to the National TB control programs (NTPs) because drug-resistant TB is much more difficult and costly to treat than fully drug-susceptible TB. It is estimated at 450,000 cases of multidrug-resistant TB (MDR -TB) occur each year among new and previously treatedTB cases, and extensively drug-resistant TB (XDR -TB) has been reported frommany countries including South Africa. Drug resistance is more common in settings where cure rates are low, for examplewhere anti-TB drugs are available without medical prescription. For this reason the NTPs have been advised over the years to focus on achievinghigh cure rates, optimizing the quality of and access to anti-TB drugs, increasing case detection rates, ensuring good treatment outcomes for patients with MDR or XDR -TB and, in settings where HIV is prevalent, on ensuring that TB patients are tested for HIV and that people with HIV are examined for TB.

2.5 Direct Observed Treatment (DOT)

Direct observation of treatment is an important element of the first component of the Stop TB Strategy. DOT means that a trained health care provider or other designated individual, including family members, observe the patient when swallowing tablets. The importance of DOT is to ensure that a TB patient takes the right drugs, in the right doses, at the right intervals and this ensures that the patient finishes treatment within the required duration, which helps to prevent transmission of the disease to others and hence reduce the chance of treatment failure and relapse.

2.6 Standard TB treatment regimens

Treatment of TB use standardized regimen, this means that all patients in a defined group receive the same treatment regimen. Standard regimens have several advantages over the individualized prescription of drugs, these include:

- Reduces likelihood of prescription errors, thus reduce risk of drug resistance.
- Facilitates estimation of drug needs, purchasing, distribution and monitoring.
- Facilitates uniform staff training.
- Reduced costs.
- Ease of maintaining a regular drug supply when patients move from one area to another.
- Make it easier for outcome evaluation and comparable results.

2.5.1 Available first-line anti-TB drugs

Based on WHO recommendations, currently, there are five essential first-line anti-TB drugs for adults and children. The drugs are formulated in fixed dose combinations (FDCs).

Individual dosages are shown belowin **Table 3**.

Dener	Recommended daily dose		
Drugs	Dosage and Range(mg/Kg body weight)	Maximum (mg)	
Isoniazid (H)	5 (4-6)	300	
Rifampicin (R)	10 (8-12)	600	
Pyrazinamide (Z)	25 (20-30)	1,600	
Ethambutol (E)	15 (15- 20)	1,100	
Streptomycin (S)	15 (12-18)	1,000	

 Table 3: Recommended daily doses of first-line anti-TB drugs for adults

2.5.3 Fixed-dose combinations

First-line anti-TB drugs are usually supplied in a form of blister packs. Each blister pack contains 28 tablets and each box of blister packs contains 24 blisters of four-drug FDCs (RHZE), which is enough for an average of four adult patients during the intensive phase. FDCs are colour coded. The FDC dosage is given based on individual's body weight (**Table 4**).

Note: Newly diagnosed adult TB patients should receive a six-month regimen containing rifampicin (**2RHZE/4RH**): The drugs should daily be taken under observation by a health care worker or treatment supporter throughout the six months.

	Body weight	Number of tables in the initial phase: 2 months	Number of tables in the continuation phase: 4 months
		(R 150/H75/ E 400/E275)mg	(R150/H75) mg
	21 – 30 kg	2	2
	31 – 50 kg	3	3
	51 – 74 kg	4	4
	≥75 kg	5	5

Table 4: Daily dosage of TB drugs in relation to body weight for FDCs in new adult TB patients

R= Rifampicin; H = Isoniazid; Z = Pyrazinamide; E = Ethambutol

Note: All patients who are rifampicin resistant should receive MDR -TB treatment in a designated health facility or clinic.

2.7 Treatment of paediatric TB

For treatment of children diagnosed with TB, treatment will depend on the availability of paediatric formulation, when not available adult formulation is used based on the Doctor's descriptions and child's body weight. The recommended type of drugs and duration for treatment of children is shown below on **Table 5**.

C C			
TB disease group	Intensive phase	Continuation phase	
All forms of PTB and EPTB except TB meningitis and TB of thespine/bone/joints	2 RHZE	4 RH	
TB meningitis, miliary TB, TB of the	2 RHZE	10 RH	
spine/bone/joints			
Previously treated smear- positive PTB (relapse, return after default, treatmentfailure)	2 RHZE	5 RHE	

 Table 5: Recommended treatment regimens for children

R= Rifampicin; H = isoniazid; Z = Pyrazinamide; E = Ethambutol

The two tables below (**Table 6 and Table 7**) show the recommended regimen and dosage for treatment of children.

Note: If the paediatric formulation is not available, the health care provider will need to give clear instruction to the parent or caregiver on how to cut and crush adult tablets to achieve the prescribed dosage.

	Intensive phase (2 months)		Continuation phase (4 months)
Weight in kg	RHZ 60/30/150 mg	Ethambutol 100mg	RH 60/30 mg
2 - 2.9	¹ / ₂ tablet	¹ / ₂ table	¹ / ₂ tablet
3 - 3.9	1 tablet	½ tablet	1 tablet
4 - 5.9	1 tablet	1 tablet	1 tablet
6 - 7.9	1.5 tablets	1.5 tablets	1.5 tablets
8 - 10 .9	2 tablets	2 tablets	2 tablets
11 - 13.9	3 tablets	2 tablets	3 tablets
14 - 19.9	4 tablets	3 tablets	4 tablets

Table 6: Weight-based dosing of anti-TB drugs for children (2-20 kg body weight)

RHZ = Rifampicin Isoniazid and Pyrazinamide; RH = Rifampicin and Isoniazid

Table 7: Weight-based dosage for children using adult anti-TB drug formulations

	Intensive phase	Continuation phase
Weightin	(2 months)	(4 months)
weight in kg	RZHE 1500/75/400/275 mg	RH 150/75 mg
5 - 5.9	¹ / ₂ tablet	¹ / ₂ tablet adult
10 - 14.9	1 tablet	1 tablet adult
15 - 19.9	1 ^{1/2} tablets	1 ^{1/2} tablets adult
20 -24.9	2 tablets	2 tablets
25 - 29.9	2 ^{1/2} tablets	2 ^{1/2} tablets
30 - 40	3 tablets	3 tablets
>40	4 tablets	4 tablets

Section Three: Management

3. Management of Tuberculosis (TB)

3.1 Introduction

Management of TB patients encompasses identification, diagnosis; initiation of treatment, assurance of available drug supplies, adherence to treatment, monitoring of drug intake as well as making sure that the patient is cured or complete treatment. Proper management of TB patients within the existing health system has become very difficult due to several factors, such as: increased number of TB patients, inadequate health personnel and limited coverage of public health services. The later has continued to impede accelerated access to TB control services (WHO 2008). Inadequate health services infrastructures, insufficient decentralization

of diagnostic and treatment services and inadequate human, material and financial resources have also contributed to poor management of patients. In additional, the direct impact of the HIV epidemic has led to an exponential increase of TB incidence, increasing pressure on hospital and public health services already stretched by the need to ensure effective delivery of essential packages of health care services (WHO 2008).

In order to address some of these challenges, several efforts have been made by different organisations including; WHO, Ministry of Health, National TB control programs (NTPs), civil society organizations (CSOs) and partners through involving community in the delivery of TB control services all aiming at better TB management, treatment adherence and better treatment outcome. For the effective engagement of communities in TB control activities, (TB care and management), guidelines and manuals have been developed by WHO including; "ENGAGE –TB"operational manual (WHO 2012) as well as training manuals on how to engage the community, NTPs (PCT manual 2005) and by other non-government organisations and civil society organisation in the delivery of TB care and management.

3.2 Involvement of community in TB treatment and management

A community consists of people living together in some form of social organization and cohesion. Although it may vary significantly in size and socioeconomic profile, its members usually share social, cultural, economic characteristics as well as common interests, including health.

The challenges posed by major epidemics such as HIV/AIDS, TB and malaria, and the role civil society has played in helping individuals and families to cope with them, have certainly contributed to make people and health policy-makers more aware of the essential and complementary role that communities can play in ensuring high-quality patient care. Community participation in TB control highlighted that a sphere of close friends and neighbours plays an important role in every person's daily life and acts as an immediate point of reference for help and advice.

Advantages of community involvement in TB care and management: Involvement of communities in the management of TB control activities has shown a significant contribution in terms of; case finding and treatment adherence, cure rate, reduction in defaulters (Egwaga, 2009), death as well as reduction of workload to the health care workers (HCWs). Community involvement facilitate access by bringing services to people's homes, and reducing the cost of care-seeking for patients and health services (WHO TB Strategy 2008, WHO 2012). Involvement of community initiatives facilitates patient and community empowerment. Through the involvement of local communities, education on relevant health issues and stimulation of change in health-related behaviour, communities become increasingly knowledgeable and self-reliant (WHO 2008).

Community engagement is critical to improve the reach and sustainability of TB interventions, helping save lives from this top infectious killer. Engagement of communities and civil society organizations in TB care is one of the core components of the End TB Strategy. The ENGAGE-TB approach aims to better identify and treat people with TB by integrating services into community-based work of previously unengaged nongovernmental and other civil society organizations. ENGAGE-TB approach seeks to shift the global perspective of TB from only a medical illness to a more comprehensive socioeconomic and community problem. The approach emphasizes the value of collaboration and partnership between NGOs and other CSOs and the NTPs. The ENGAGE-TB emphasizes among other things in TB monitoring and reporting, in order to ensure that national data is adequately captured the contribution of community-based TB activities is evidently.

Section 4: Challenges

4. Challenges in Treatment and Management of Tuberculosis

Despite that there have been great achievements in the treatment and management of TB both in terms of high treatment success rates and integration of TB-HIV care and management there are still several challenges. Below are some of the challenges in terms of treatment, management among TB, TB/HIV co-infected and in special situations (MDR-TB and prisons).

4.1 TB Treatment challenges

- At times the NTPs experience drug interruption due to inadequate or limited supply of 1st line anti-TB drugs.
- Long TB treatment duration of (6-8 months).
- Irregular treatment; i.e. treatment failure, drug resistance and relapse.
- Coping strategies for difficulties of "real" DOT: since health care workers cannot coup to daily observe the TB patients taking drugs at the health facility, communities are engaged to observe patients taking drugs at their homes. Involvement of lay persons in the communityor in the family is a challenge; In **community:** Issues of accountability, confidentiality, remuneration, and sustainability, In **family**: DOT is rather a disguised self-administered treatment.

4.2 TB/HIV co-infection challenges

About 40–65% of HIV-infected African patients with respiratory disease have TB.

- Weakened health system due to inadequate number of health care workers and increased

number of patients to be managed (TB-HIV co-infected).

- Health care delivery is weakened due to absenteeism of staff because of illness.
- TB control programmatic delivery and patient management are adversely affected by HIV epidemic.
- Increased risk of drug toxicities
- Higher pill burden
- Drug interactions when anti-TB and anti-HIV treatments are taken together
- Occurrence of immune-reconstitution syndrome

4.3 Programmatic delivery challenges

- Health services struggle to cope with increasing numbers of TB suspects and patients
- Stock-outs of sputum containers as the demand fails to keep pace with supply frequent
- More smears have to be prepared and examined with risk of increase false-negative results.
- Paradoxically, with increase in TB burden due to HIV, case detection rates for smear positive PTB decline.

4.4 Patient management challenges

The following are some of the challenges that adversely affect the image of the TB program

- Diagnosis of TB more difficult in HIV infected persons:
- Clinical picture and radiological findings are atypical
- More patients likely to die during the course of treatment
- High early case fatality or more deaths during the first two months of anti-TB treatment and higher rate of recurrent TB among HIV+ compares to HIV- patients.

4.5 Other challenges are those in special populations including; Patients with MDR-TB and prisoners with TB

For MDR-TB challenges include;

- Management of MDR-and XDR-TB is complex and expensive
- 2nd line medications not routinely available
- Treatment of MDR-TB is long, expensive with many side-effects and requires special dispositions for follow-up and care
- For prisoners with TB challenges include;
 - Overcrowding
 - Poor ventilation of cells
 - Malnutrition
 - Higher rates of HIV than in general population
 - Hygiene and health services sub-standard or inexistent
 - TB in prisons affects the general population through transmission when prisoners are released and via prison staff and visitors.

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