Review Article

Tuberculosis: A review of current concepts and control programme in Nigeria

1. **Dr. Cyril C. Dim, M.Sc, FWACS, FMCOG**
Erasmus Mundus Scholar of International Health; Departments of Physiology/Obstetrics & Gynaecology, University of Nigeria, Enugu Campus, Nigeria; Honorary consultant Obstetrician & Gynaecologist University of Nigeria Teaching Hospital (UNTH), Enugu;
2. **Dr. Ngozi R. Dim, MPH**
Department of Radiation Medicine, UNTH, Enugu, Nigeria
3. **Prof. Odd Morkve, MD, PhD**
Center for International Health (CIH), University of Bergen, Norway

ABSTRACT

BACKGROUND: The burden of tuberculosis in Nigeria is the highest in Africa. Therefore, improved knowledge of health workers on the current issues concerning the disease, including the National guideline, is important for effective disease control.

METHODS: An in-depth search of relevant literature on the subject area. This includes texts and operational documents of the Nigerian national tuberculosis programme, as well as online searches using Pubmed, African journal online (Ajol), and Google scholar.

RESULTS: About one third of the world population is infected with tuberculous bacilli with up to 10% lifetime risk of developing the disease. Pulmonary tuberculosis (PTB) especially the reactivated latent infection is the major source of the infection in communities. In an effort to increase case detection, a single acid fast bacillus in at least one of two sputum smears is currently adequate to diagnose PTB. Furthermore, there is a global effort to eliminate the disease by the year 2050 and these efforts are coordinated in Nigeria by the National tuberculosis control programme.

CONCLUSION: Tuberculosis is an impediment to human development in developing countries, especially in this era of HIV pandemic. Continuing education of health professional on tuberculosis and its accessible treatment, will improve patients' education, proper management and appropriate referral.

INTRODUCTION

Tuberculosis(TB) is an infectious disease whose scourge has been with humans throughout known history.[1] About one third of the over 6 billion world population is estimated to be infected with the disease-causing organism, and the lifetime risk of developing the disease, for each person, can be over 10%.[2] It is therefore a global pandemic whose impact on world development is well recognized which made the United Nations (UN) to define TB-specific indicators for monitoring her target of reversing the incidence of major diseases by the year 2015.[3] Though TB is curable, about 4500 people die of the disease daily and it is noteworthy that most of these deaths occur in developing countries where poverty, malnutrition, and HIV/AIDS are also prevalent.[4] In response to the huge burden of TB, a major effort towards global control of the disease was initiated through the widespread implementation of the *DOTS* strategy, and this effort is being consolidated and enhanced through the *Stop TB Strategy*.[5] The four main targets of this global control are: the fall of TB incidence by the year 2015; the reduction of TB prevalence and death by half by 2015 when compared to their levels in 1990; the detection and treatment of at least 70% of the estimated incident cases in DOTS programme; and finally, the successful treatment of at least 85% of incident smear-positive cases.[6] Furthermore, TB is a disease of international health concern and research findings, guidelines and concepts continue to emerge. The fight against the disease could be enhanced through the dissemination of appropriate information to health workers especially in Nigeria which ranked 4th in the global list of high disease burden countries.[6] This review offers a concise discussion of the current knowlegde on the history, aetiology and transmission of TB; diagnosis and treatment of TB with emphasis on Nigerian national guideline; and the global / national burden of TB. Also, the structure of the National TB control programme as well as the main definitions used in TB management in Nigeria are highlighted.

AETIOLOGY OF TUBERCULOSIS

TB is caused by the infection with tubercle bacilli - a generic name that incorporates an expanding list of *Mycobacterium* species collectively called *Mycobacterium tuberculosis complex*. Members of this group are: *Mycobacterium tuberculosis*, *M. bovis, M. africanum, M. microti, M. canetti, M. caprae, and M. pinnipedi.*[7;8] They are generally facultative intracellular pathogens which may be related to their long period of persistence in individuals with latent TB.[7] Also, they are obligate aerobes therefore; grow better in oxygen rich tissues such as the lungs which may explain why the majority of the disease cases involve the lungs. However, despite their high degree of DNA similarity, *M. tuberculosis* is the major cause of human tuberculosis.[9]

***Correspondence to:** Dr. Cyril Chukwudi DIM, Departments of Obstetrics & Gynaecology, UNTH, P.M.B. 01129, Enugu. 400001- Nigeria.
Telephone: +234 8033341960 E-mail: dyme72@yahoo.com

Molecular typing of *M. tuberculosis complex* among TB patients in Nigeria showed that in the majority of cases, the disease was caused by *M. tuberculosis* followed by *M. africanum,* while *M. bovis* contributed the least.[10]

HISTORY OF TUBERCULOSIS

TB seems to have been a global public health problem for many centuries as shown by its global afflictions and impacts.[1] Despite the lack of archaeological evidence, the causative organism is hypothesized to have originated from East Africa.[1] Nevertheless, the identification of classical skeletal features of the disease,[11] and the amplification of *M. tuberculosis* DNA in Egyptian mummies,[12] are pointers to the possible devastating impact of the disease in ancient Africa.

The isolation of the tubercle bacillus in 1882 by Robert Koch gave hope to the control of an almost evasive disease. Furthermore, the development of streptomycin, isoniazid, and rifampicin in the mid 20th century introduced a new and effective regime for treatment of TB; prior to then, several treatment strategies with unconfirmed effectiveness such as rest (in sanatorium), exercise, and pulmonary collapse strategies, had been employed.[1;13]

The only available vaccine for TB is *Bacille Calmette Guerin* (BCG). It is made of live attenuated *M. bovis,* and was first used in 1921.[14] Incidentally, the vaccine neither prevents primary infection nor the reactivation of latent pulmonary infection which makes it useless for the much needed primary prevention of TB.[15]

Furthermore, the Directly Observed Therapy Short-course (DOTS) was introduced in Nigeria in 1993 by the *German tuberculosis/leprosy Relief Agency* (GLRA), and implementation was expanded to all States of the Federation in 2004.[16]

TRANSMISSION OF TUBERCULOSIS

TB is a chronic infection with predilection for the human lungs (pulmonary TB) but, it can affect any other organ of the body (extra-pulmonary TB).[16] The causative organisms are transmitted through the inhalation of airborne droplet nuclei generated from individuals with the pulmonary disease.[17] Following the infection, any of these outcomes may result thus: the bacilli may be killed by the host immune system; they may proliferate and cause primary TB; they may be dormant and remain asymptomatic (latent infection); or they may be reactivated after a period of latency.[18] It is estimated that about 5-10% of persons with latent infection will develop TB during their lifetime but the risk is higher among children and the immunocompromised such as HIV/AIDS.[17] Also, an average of 10-15 persons are estimated to contract the infection annually from one infectious pulmonary TB case.[15]

A lot of host and environmental factors interact to predispose individuals to TB; the independent risk factors identified in West Africa include family history of TB, household crowding, male sex, HIV infection, smoking - the latter had a dose-response relationship with TB,[19] and therefore should stimulate further studies. A related study in Gambia had also identified ethnicity as a risk factor but explained that it could be due to the underlying environmental and behavioural factors.[20] Furthermore, a recent study from Tanzania showed that though patients with prolonged duration of cough (two or more weeks) had a higher likelihood of being diagnosed with TB when compared to those with shorter duration of cough, the relationship was not significant [OR = 1.6 (95% CI: 0.59, 4.49)].[21] In Nigeria, the inefficient health system is believed to be perpetuating the cycle of disease-poverty-disease of the majority of Nigerian,[22] and this theory definitely applies to TB.

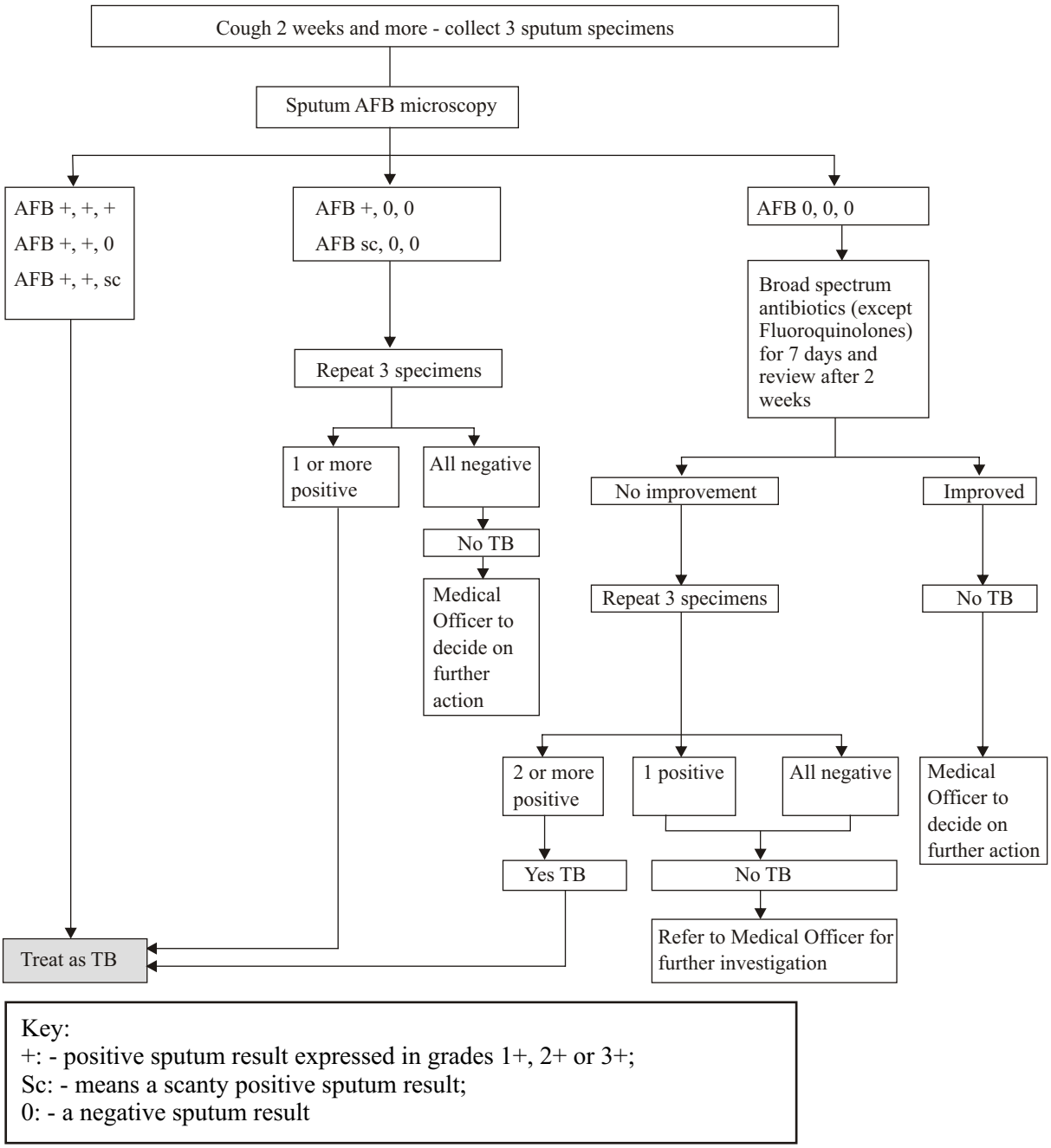
DIAGNOSIS OF TUBERCULOSIS

TB can affect any organ of the body but the pulmonary TB especially the reactivated latent infection is of most public health concern because it is the major source of tubercle bacilli spread in the communities.[15] Further reviews will therefore be restricted to PTB.

Generally, the diagnosis of TB is based on "possible exposure, a typical disease history, suggestive clinical findings, typical radiological changes and positive bacteriological tests."[15] Sputum smear direct microscopy and conventional solid media culture are the most widely used laboratory diagnostic methods in the global TB control. However, most diagnoses of TB are based on the smear microscopy for acid-fast bacilli (AFB). The technique is fast, accessible, and specific but it is limited by its low and variable sensitivity and the inability to detect drug resistant bacilli.[23] Because of the progressive improvement of the quality assurance programmes for smear microscopy, WHO has redefined a new sputum smear-positive PTB as the presence of single AFB in at least one sputum smear examination from a TB suspect.[23] Likewise, the number of smears required for the diagnosis of PTB has been reduced to two.[23] This decision considered the barriers of accessing TB control services in resource poor setting including laboratory workload, as well as the incremental diagnostic yield of 3 serial sputum specimens; and hoped that the new policy would enhance case detection through improved "quality of service, decreased time for diagnosis and initiation of treatment and decreased patients drop out from the diagnostic pathway".[23]

The national tuberculosis programme in Nigeria relies on direct microscopy for diagnoses of PTB (Fig. 1), and is yet to adopt the new WHO policy on new smear positive PTB.[24]

Figure 1: A flow chart for the management of TB suspects in Nigeria.[24]



TREATMENT OF TUBERCULOSIS

BCG vaccination and chemoprophylaxis are unsatisfactory TB control measures thereby leaving anti-tubercular (anti-TB) chemotherapy as the only option.[25] The essential (first-line) anti-TB drugs are isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), and streptomycin (S).[5] Their use in combinations (multi-drug therapy) is aimed at achieving cure without relapse, preventing death, impeding transmission by depleting infection source pool, and preventing the emergence and transmission of drug resistance.[5;25] The fixed-dose combinations (FDCs) have equivalent efficacy to separate-tablet combinations[26] and are therefore preferred because of several advantages such as increased patient acceptance, discouragement of selective ingestion of the drugs and possible monotherapy, and prescription error.[5] Other strategies introduced to improve TB treatment are the "patient kit" which ensures that the full treatment for a patient is available for the desired treatment duration; the "standard regimen" which introduced a standard (same) treatment for each patient registration group (category).[5]

The standard therapies of TB are usually divided into 2 phases, an initial intensive phase followed be a continuation phase. For new patients, the regime (2HRZE/4HR) consists of an intensive phase of

rifampicin, isoniazid, pyrazinamide, and ethambutol daily for 2 months, and a continuation phase of rifampicin and isoniazid for a further 4 months, preferably daily or 3 times per week.[5] Thrice weekly regime throughout the course of the treatment is an acceptable alternative in non HIV-prevalent areas provided that treatment is directly observed.[5] This therefore implies that Nigeria with an HIV/AIDS prevalence rate of 3.1% as at 2007,[27] is not eligible to use this alternative regime. Furthermore, in settings with proven or unknown isoniazid resistance level, HRE instead of HR should be used at the continuation phase. The isoniazid resistance status (new cases) of Nigeria is assumed to be low. This is supported by a very small sample study from Jos, northern Nigeria which did not identify isoniazid resistance in both new and follow-up cases.[28] Nevertheless, this report contrasts an earlier and equally small sample study from a similar region which reported an isoniazid resistance of 6.6% among new cases.[29]

The DOTS in Nigeria uses 2HRZE/4HR or 2HRZE/6HE regimes for category 1 (new cases) 6HE is self administered while 4HR therapy should be observed daily.[24] For retreatment cases (category 2), the 2SRHZE/1RHZE/5RHE is used.[24] The current WHO guideline recommends that all re-treatment cases undergo specimen culture and drug sensitivity testing (DST) for at least isoniazid and rifampicin before treatment if the Rapid molecular-based DST is available; otherwise standard empirical treatment (category 2) should be commenced and modified with the result of the conventional culture when available.[5] The recommendation is in response to the report of the *Global Project on Anti-tuberculosis Drug Resistance Surveillance* which showed a high global mean multi-drug resistance (MDR) of 15.3% [95% CI: 9.6-21.1] for previously treated cases and 2.9% [95% CI: 2.2-3.6] among new cases.[30] For the African region, the report showed a mean MDR of 1.5% [95% CI: 1.0-2.0] for new cases, and 5.8% [95% CI: 3.9-7.7] for previously treated cases.[30] This apparent low level of MDR-TB gives hope to the control of TB in this continent where poverty, hunger and HIV are endemic. However, the current workers' manual used in Nigeria suggests that the WHO recommendation is only observed after treatment attempts at the category 2 level thus: "for patients who remain positive after category 2; continue RHE medication, inform the Local government TB supervisor (LGTBLS) or State TB control officer (STBLCO), and refer to medical officer for sputum culture, sensitivity test and appropriate treatment"[24]

MDR-TB in Nigeria is apparently low - the estimate for 2007 was 1.8% for new cases and 9.4% for retreatment cases.[6] Also, the study in Jos, reported an MDR of 4% among new cases and 18% among the follow-up cases,[28] while another study from a referral center in Ibadan, South-western Nigeria showed an MDR of 53.6% among new patients though over half of the cases were from the anti-retroviral clinic of the hospital.[31] The obvious disparity between the two studies calls for a well designed nationwide survey to determine the true picture of anti-TB drug resistance.

On the other hand, a study in Enugu, Nigeria among chronic TB patients referred by the national TB programme for category 2 related problems (failure, relapse, and returning defaulter with smear positive result), showed an MDR-TB of 72%, and poly-drug resistance of 25.6% while one patient each showed sensitivity to all drugs and isoniazid mono-resistance respectively.[32] The study however has questionable internal validity because 33% of the study participants were excluded from analysis for various reasons.[32]

GLOBAL BURDEN OF TUBERCULOSIS

According to the WHO estimates for 2007,[6] all incident cases of TB was 9.27 million as against 9.24 million in 2006, and 6.6 million in 1990. Most of the cases were from Asia (55%) and Africa (31%) while the least estimate was from the Americas (3%). Fifteen percent of the 9.27 million incident TB cases were co-infected with HIV and Africa contributed 79% of them. The high burden of TB in Asia and Africa is reflected on the WHO list of high TB burden countries which was topped by five countries from these regions.

The estimated prevalent cases decreased from 13.9 million (210 per 100 000 population) in 2006, to 13.7 million (206 per 100 000 population) in 2007. Also, the estimated deaths from TB was 1.3 million among HIV-negative new TB cases (20 per 100 000 population) and 456 000 among new TB cases who were HIV-positive. Half a million TB cases were estimated to be MDR-TB in 2007; and by the end of 2008, 55 countries had reported extensively drug resistance TB (XDR-TB). The case detection rate for new smear-positive cases for 2007 was 63% which was still lower than the DOTS target of 70%.

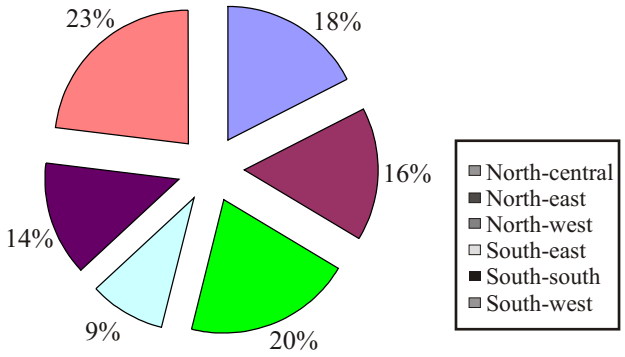
NATIONAL BURDEN OF TUBERCULOSIS

In year 2007, Nigeria ranked fourth in the world and first in Africa with respect to the WHO estimated number of TB cases.[6] Unfortunately, a 2008 report estimated the total TB cases in Nigeria as 922,575, and was ranked 3rd (behind India and China) on the list of high-burden countries.[33] Furthermore, as at 2007, the WHO estimated that Nigeria had 460,000 cases of all forms of TB, a TB prevalence of 521/100,000 population, 195,000 new smear positive cases, incidence rate (all cases) of 311/100,000 per year, and incidence rate (new smear positive) of 131/100,000 per year.[6] Further estimates include the prevalence of all forms of TB in HIV of 42/100,000, and a death rate of 93/100,000 population per year (138,000 deaths/year).[6]

However, the most recent national TB report[16]

showed that since 2002 when nation-wide expansion of DOTS started, only 455,552 of TB (all forms) have been registered; out of which 92.2% were new cases and 7.8% were retreatment cases. In 2008, a total of 90,311 TB cases (92% new cases, 8% retreatment cases) were registered; notably, the sputum smear positive (ss+) cases contributed only 51% of the new cases. The reported new ss+ PTB cases represented only 30.5% of the estimated new ss+ for the year but, nearly doubled the detection rate of 16 % in 2002. The TB cases per State of the Federation for the same year, ranges from 721 cases in Ekiti to 9,864 cases in Lagos. The South-eastern zone contributed the least (9%) number of cases (Fig. 2).

Figure 2: Annual TB cases by zones of Nigeria for year 2008,[16]



NATIONAL TUBERCULOSIS CONTROL PROGRAMME OF NIGERIA[16]

The national TB control activities in Nigeria are coordinated by the *National tuberculosis and leprosy control programme* (NTBLCP) which was launched in February 1991 under the department of Public health in the Federal ministry of health (FMOH). Its basic disease control strategy is the provision of free services to all patients identified with TB and its operations are guided by DOTS strategies and *STOP TB Partnership* initiatives.

NTBLCP is structured along the three tiers of Nigerian government thus the Federal, State, and Local government areas (LGAs). Each level provides technical and management support to the one directly below it for instance, the Federal (National) programme supports the States' TB control programme. Furthermore, the Federal level is also in charge of policy development, tertiary patient care, mobilization and development of human and material resource. The States' TB programmes are responsible for coordinating TB control activities within the States, and provision of secondary patients' care. The operational level of the national TB control programme is the LGAs and it is based on the principles of Primary health care (PHC). At least 2 health centers in each of the 774 LGAs in Nigeria have fully functional DOTS services.[6]

NTBLCP re-defined its strategies in 2006 and developed the following specific targets to be achieved by the year 2010 thus: to detect 70% of the estimated smear positive TB; to successfully treat at least 85% of all detected TB cases; to ensure a minimum of 80% implementation rate of the programme's activities by strengthening the technical and managerial capacity of the NTBLCP; to promote behavioural change in the community about TB such that 70% of adult population become aware of TB, its prevention, and the available free treatment as well as motivate the at risk groups to seek for immediate care; to reduce the incidence of TB among HIV patients by 25%. It is hoped that some success have been achieved as regards to these targets.

MAIN DEFINITIONS FOR TUBERCULOSIS REGISTRATION

The definitions for different categories of TB patients and the treatment outcome by the national TB control of Nigeria are listed in tables 1 and 2.

Table 1: Definitions for registered sputum smear positive TB patients in Nigeria.[24]

Category	Definition
New case	A patient who has never had treatment for TB or who has taken anti -TB drug for less than 4 weeks.
Relapse	A TB patient who previously received treatment and was declared cured or completed a full course of treatment and has once again developed sputum smear-positive TB
Treatment failure	A smear positive patient who while on treatment remained, or became smear positive again *five months or later* after starting treatment
Treatment after default	A TB patient who completed at least four weeks of Category 1 treatment and returned smear positive after at least 8 weeks of interruption of treatment
Transfer in	A TB patient already registered for treatment in one LGA/State who is transferred to another LGA/State where s/he continues treatment.
Other	All cases that do not fit the above definitions. This group includes: ☐ Chronic cases patients who remains smear positive after completing re-treatment regimen(cat 2) ☐ A patient treated for TB outside the DOTS for more than four weeks and is smear-positive. ☐ A patient diagnose as sputum smear negative TB after a cure or successful treatment ☐ A patient who previously received treatment but outcome of treatment is un-known and now smear positive.

Table 2: Recording treatment outcome in smear-positive TB patients.[24]

Cured	A patient who was smear -positive at diagnosis, who completed 6 or 8 months of treatment and who is smear-negative at the end of 6th or 7th month of treatment and on at least one previous occasion.
Treatment completed	Any patient who was smear -positive at diagnosis and who completed treatment but in whom smear examination results are not available at the end of treatment.
Treatment failure	Any patient who remains or becomes smear positive again at the end of fifth month or later during chemotherapy
Treatment success	the sum of patients cured and those who have completed treatment
Died:	Any patient who dies for any reason during the course of his/her chemotherapy.
Defaulter:	Any patient whose treatment was interrupted for 8 consecutive weeks or more after the date of the last attendance
Transferred out [a]	A patient who has been transferred to another treatment centre in another State and whose treatment result is not known. Note: trans ferred out is not allowed within the same State; rather the patient can be referred to another LGA and his treatment outcome obtained during the quarterly review meeting

[a] **The LGTBLS should obtain the outcome of every patient, including those that were referred to another health facility if possible.**

CONCLUSION

Tuberculosis remains a huge challenge in developing countries, especially in this era of HIV pandemic. The burden of the disease in Nigeria is the highest in Africa and efforts at controlling the disease are coordinated through the NTBLCP which has well defined programme objectives and targets. Continuing education of health professional on tuberculosis and its current treatment guidelines as well as the existence of functional DOTS centers in all LGAs of the country, will improve patient education, proper management and appropriate referral.

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