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Review Article

An Overview of Prospect and Challenges in Achieving End Tb Strategy Of 2030 - 2035; North Central Zone Nigeria, As A Focus: A Review.

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ABSTRACT

The Mycobacterium tuberculosis (M. tuberculosis) complex is one of the oldest recognized human harmful infectious diseases, it is one of the single greatest infectious disease killers in the world, and has been declared a worldwide emergency. The review study is aimed at determining the effectiveness of the treatment, management, control and prevention of tuberculosis inachieving End TB strategy 2030-2035 in north central zone of Nigeria. In this retrospective review study, scientific literatures in electronic database of Google scholar, Pub Meds, and Scopus using search themes as tuberculosis, prevalence, risk factor, transmission and treatment were retrieved and examined. The incidence and prevalence of TB is not well documented in Nigeria, due to the fact that majority of individuals with the disease are not captured as a result of many being latent carriers of TB. Inability to properly diagnose the condition due to poor and inadequate infrastructures, lack of resources to provide the latest diagnostic services, lack of well-trained staff in the knowledge of the diagnosis of TB, accurate and reliable methods of diagnosis such as Interferon-gamma release assay (IGRA) has been a challenge in the North Central Zone(NCZ) of Nigeria. Latent carrier of TB due to inability to diagnose them and offer treatment is a huge challenge that could impede the policy of End TB Strategy 2030-2035. The health facilities where TB cases are managed should put in place adequate resources and well trained man power that would be able to provide accurate diagnosis to ensure proper treatment; these will facilitate early and complete eradication of the disease in NCZ and Nigeria; thereby achieving End TB Strategy 2030-2035.

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Introduction

Tuberculosis is the greatest infectious disease killer in the world, tuberculosis (TB) has a severe impact on populations that are more susceptible. When tuberculosis (TB) was declared a worldwide emergency in 1994, several tried-and-tested solutions were introduced to treat and manage the condition, including the Directly Observed Treatment Short course(DOTS) strategy (1994–2005), the STOP TB partnership plan (2006–20015), and the End TB strategy (2030–2035). Nevertheless, despite improvements in the number of lives saved between 2000 and 2020, the path to global tuberculosis control appears to be far off [1].

The United Nations High Level Meeting on TB in 2018, which was attended by heads of state, is evidence of the threat that unchecked tuberculosis transmission poses to modern society [2] Nigeria is a nation with high rates of TB, TB-HIV co-infection and multidrug-resistant TB (MDR-TB) cases [2].

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The World Health Organization (WHO),2019, global tuberculosis report states that Nigeria reported 106,533 cases of tuberculosis in 2018, which translates to 38% estimated mortality/incidence ratio. The nation's high rate of HIV infection, severe poverty, poor and inadequate healthcare infrastructure, and other factors have all contributed to the spread of new tuberculosis infections TB. [3, 1]. Of the eight countries that accounted for two thirds of the cases of tuberculosis globally, Nigeria ranked as number one.

Nigeria is divided into six geopolitical zones, with the North Central Zone (NCZ) being one of the zones with high incidence of TB. The NCZ consists of the Federal Capital Territory as well as these other six states (Benue, Kogi, Kwara, Nasarawa, Niger, and Plateau).

In 2018 the National TB Control Program (NTP) for Nigeria notified the WHO of fifteen thousand six hundred and twenty-seven (15, 627) TB cases (all types), which represents 14.6% of all TB case notifications. Thirty-one million three hundred and eleven thousand four hundred and fifty-two (31,311,452) people live in the zone, where there are 6,861 health institutions in total; with 1,508 (22.0%) medical facilities, and TB Directly Observed Treatment Short course (DOTS) available. The Local Government Area (LGA) coverage for microscopy and the gene-Xpert MTB/RIF assay for health facilities in 2018 was 529 (7.7%) and 98 (53.7%), respectively.

Therefore, it is clear from the above data, that the zone has limited TB service coverage. Early TB diagnosis and treatment for those afflicted are critical steps in the control of TB, and they work in concert with the WHO End TB strategy. In comparison to the anticipated TB burden for the zone of 371/2800 (13.25%), the number of TB cases discovered and placed on treatment in the NCZ of Nigeria is low. Thus, it is critical to address the aforementioned issues in the zone as the nation moves closer to hitting significant milestone targets for the End TB strategy.

Globally, tuberculosis (TB) is a leading cause of death from infectious diseases, particularly in young adults who are susceptible. A nation's TB burden can be accurately estimated using TB case notifications and occurrences.

Over time, there has been a steady increase in tuberculosis cases. In order to reduce the burden of disease and death caused by tuberculosis, as well as to achieve the End TB Strategy targets set for 2030 to 2035, which are linked to the Sustainable Development Goal (SDG) of reducing tuberculosis deaths to 90% by 2030, reducing new cases by 80% between 2015 and 2030, and ensuring that no family is burdened with high costs due to tuberculosis should be the primary objective. Therefore, this study is aimed at shedding light on the tuberculosis (TB) status in the six states that comprised Nigeria's North Central Zone (NCZ) between 2018 and 2023;and as well ascertain the progress made and the effectiveness of End TB Strategy. The big question in the mind of researchers, stakeholders, patients and the government are, is this End TB strategy be achievable in the North Central Zone, Nigeria.

METHODS

The present review was carried out in accordance with the preferred reporting items for systemic reviews and meta-analysis extension for scoping reviews (PRISMA-ScR) guidelines. In this review, scientific papers published in electronic database between 2010 to 2022, including Google scholar, PubMed, and Scopus were retrieved using search themes such as Tuberculosis, prevalence, Risk factor, diagnosis, Transmission, and prevention were examined. Scientific papers published in electronic databases that were unable to be downloaded were excluded in the review. The remaining references were filtered to ensure only articles covering the search themes were examined in the review.

AETIOLOGY

Robert Koch won the Nobel Prize in 1905 for proving in 1882 that the tubercle bacillus was the real cause of tuberculosis. The most prevalent and significant agent responsible for human disease within the Mycobacterium tuberculosis complex is tubercle bacilli.Tubercle Bacilli (TB) is an infectious bacterium that causes tuberculosis. Occasionally, similar related Mycobacteria, such asM. bovis, M. africanum, and M. microti, cause similar disease.

EPIDERMIOLOGY OF TUBERCULOSIS

The Mycobacterium tuberculosis (M. tuberculosis) complex is one of the oldest known human harmful infectious illnesses, and research on it is ongoing worldwide [4]. Globally, the illness has a significant influence on health and the economy. The development of treatment regimens has advanced the efforts to prevent, control and completely eliminate tuberculosis. Nonetheless, despite a lengthy history and ongoing efforts, M. tuberculosis infections continue to be a persistent global health concern. The co-occurrence of diabetes and HIV epidemics, which raise the risk of tuberculosis, together with the advent of antibiotic-resistant MDR and exceptionally drug-resistant (XDR) strains, are significant causes for concern[5].Extra-pulmonary infections have developed as a result of the causative agent's changing or mutating nature [6].

Extra-pulmonary infections account for 15% of tuberculosis cases. According to reports, these cases are extremely challenging to identify and manage, and organ transplantation is one easy way for them to spread [6]. A tuberculin skin test (TST) with a sensitivity of 89% to 95% can be used to detect TB immune reactivity and determine a positive TB diagnosis when utilizing the regular TB test (CDC, 2010). Immunological memory and recall responses are utilized as markers for tuberculosis infection, and the use of immune-reactivity as a proxy for infection is founded on the idea of the body's natural immune reaction against the TB bacterium [5]. Immunocompromised individuals are more vulnerable to tuberculosis infection and have reduced immune responses.

Again, this diagnostic strategy runs the risk of producing false negative results when the immune-compromised patient's bacteria population is low. One of the body's most important defenses against tuberculosis is cell-mediated immunity, particularly the function of CD4+ T cells [5]. This finding explains why individuals living with HIV who have compromised CD4+ immune systems are more susceptible to contracting tuberculosis. However, it has been demonstrated that HIV individuals have reduced CD4 values.

Nigeria is classified among the 14 high burden countries for TB, TB/HIV co-infection and MDR-TB. In its incidence rating of all forms of TB, it was 219/100,000 population (WHO, 2018). A total of 432 Nigerians dies daily from TB with estimated 115,000 dying each year with its case detection rate of 24% and an estimated 500,000 new cases with only 104,904 cases notified to the NTBLCP (WHO, 2018). In North Central Zone, 15, 627 TB cases (all forms) were notified in2018 accounting for 14.6% of the total TB case notification reported to WHO [7].

PATHOGENESIS

The primary cause of Tuberculosisis tubercle bacilli which are carried by air droplets; when the tubercle bacilli droplet nuclei enter the lung's alveoli, infection results. As a line of defense against the pathogen, the macrophages in the alveoli engulfed the tubercle bacilli, leading to the elimination of the pathogenic bacterium. In an instance of immunological barrier failure, which results in latent tuberculosis infection (LTBI); the pathogen propagated via lymphatic channels, the bloodstream, lymph nodes, and the apex of the lung, kidneys, brain, and bone respectively [8]. The bacteria are capable of creating intracellular cables. The pathogen's capacity to form cords and undergo mutations has enhanced its virulence and resistance to medication [9, 8]. The tubercle bacilli outcompete the immune system in immunocompromised subjects. The pathogenesis of Tuberculosis is illustrated in the diagram A, B, C and D Fig 1 below.

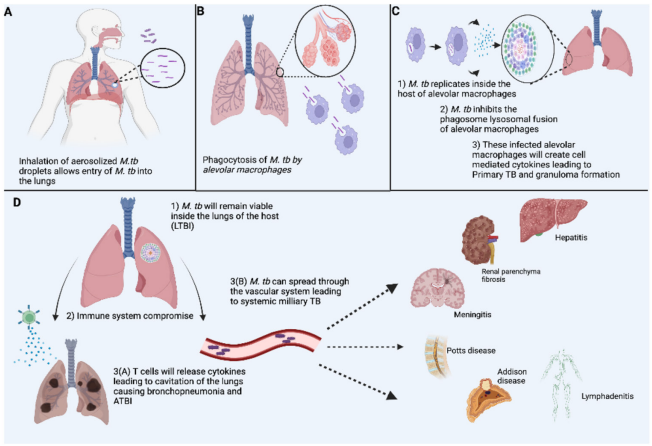


Fig 1: PATHOGENESIS OF TB, A, B, C and D, [9].

TRANSMISSION

Theairborne particles containing tubercle bacilli are released into the atmosphere or environment, when a subject with pulmonary or laryngeal TB disease cough, sneeze, shout, or sing. Several hours may pass before these particles leave the air space, depending on ventilation and atmospheric conditions. When a person inhales infected aerosols containing M. tuberculosis, transmission starts. Since direct sunlight quickly kills M. tuberculosis and ventilation eliminates droplet nuclei from contaminated spaces, this typically happens indoors, WHO2018[10].

The transmission of TB is prevalent in unvaccinated population as illustrated in Fig 2 below. Vaccination against the transmission and spread of TB should be encouraged and made a priority in NCZ, Nigeria, and all countries where TB are prevalent.

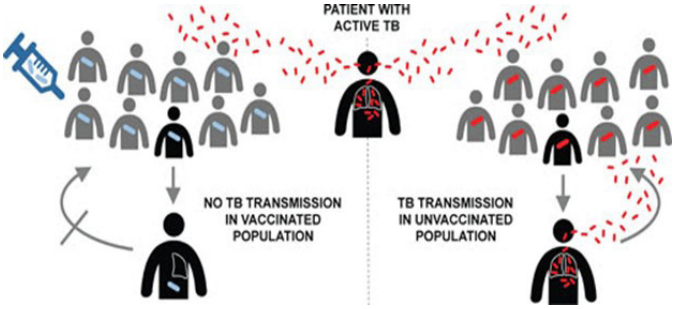


Fig 2: TRANSMISSIONN OF TB [10].

Symptoms Associated with TB

The subject with latent or inactive TB will have no symptoms, due to the fact that at this stage the bacterium is not causing harm in the patient or subject. However, the major symptoms associated with TB are as follows:

- •Cough,
- •Coughing out blood or mucus,
- •Chest pain,
- •Pain with breathing or coughing,
- •Fever,
- •Chills,
- • Night sweats and weight loss.

Risk factors

Numerous variables affect a person's risk of infection, such as the amount of M. tuberculosis in the air, The length of time spent in the air with droplet nuclei, The infectiousness or bacillary load of the patients sputum (smear positivity is a useful indicator), The room's ventilation during the exposure, Some risk factors include an individual's susceptibility to the infection; the high percentage of patients with drug-resistant TB, estimated at 4.3% among new cases and 25% among individuals that have already received treatment, is another factor contributing to Nigeria's high TB burden [11].

TB CASE NOTIFICATION RATE

According to Federal Ministry of Health, (2019), the total number of TB cases reported as of 2018 in north central Nigeria ranged from 13,352 to 2,626 cases among states. The number of new cases, relapses, and patients with no prior history of tuberculosis treatment notifications per 100,000 people increased in all states in 2019. In 2019 there were 26 new cases of TB (including TB+HIV) per 100,000 people in Kwara and Kogi, and 100 new cases per 100,000 people in Nasarawa (figure 2).

Kwara had the largest rise in the case notification rate percentage between 2018 and 2019, followed by Nasarawa at 7%, Abuja at 5%, Niger at 4%, and others at 1% apiece figure 4: FMOH,2019[12]. The most noticeable and direct result of the COVID-19 pandemic's disruptions to tuberculosis (TB) in several nations was a sharp decline in the number of newly diagnosed cases that were reported, or formally notified, in 2020. Despite this, the number of TB cases in the region continued to rise, as reported by the World Health Organization in 2022.

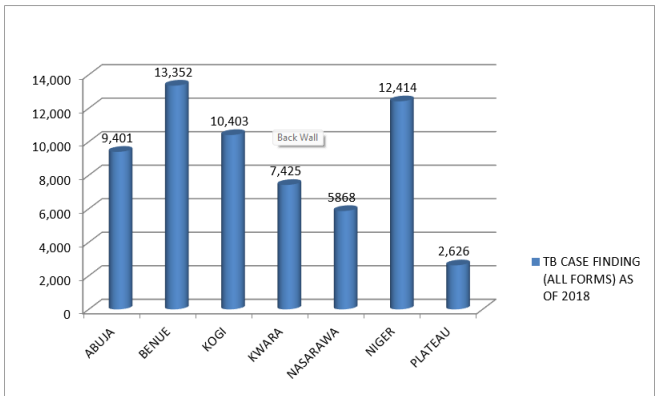


Figure 3: TB CASE FINDING (ALL FORMS) AS OF 2018 [FMOH, 2019]

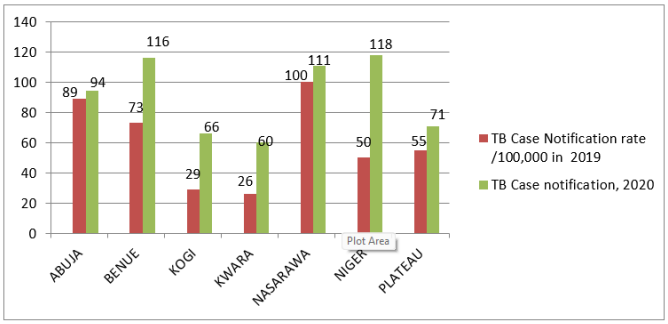


Figure 4: CASE NOTIFICATION RATE (CNR)/100,000 FOR ALL FORMS OF TB CASES IN 2019 IN NCZ [FMOH, 2019].

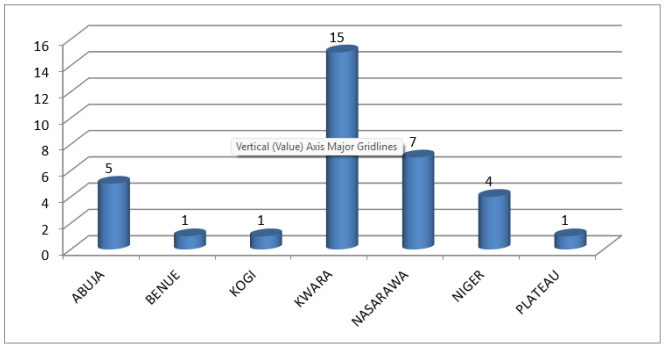


Figure 5: PERCENTAGE INCREASE IN TB CASE NOTIFICATION FROM 2018 TO 2019 [FMOH, 2019].

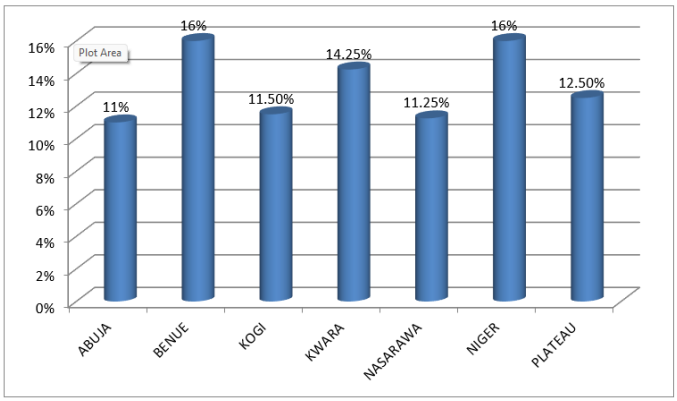


Figure 6: Prevalence of TB in North Central States, Nigeria, 2020.

LABORATORY DIAGNOSIS OF TB

Laboratory diagnoses play a critical role in the identification, isolation, treatment, monitoring of the effectiveness of treatment, control, preventionand eradication of TB in any given community. Key responsibilities of a contemporary tuberculosis laboratory include the identification of the mycobacterial species or complex that has been isolated, the susceptibility of the organism to anti-mycobacterial medications, and the detection and isolation of mycobacteria [13].

There is no gold standard method for the diagnosis of TB, [5]; however, for identifying TB microbiologically through culture is for the diagnosis of active disease. The understanding of tuberculosis epidemiology is greatly enhanced by the molecular typing of isolates. TB control efforts have been assessed by population-based genetic epidemiology investigations, which have improved contact tracing, shed light on transmission patterns, and aided in the identification of laboratory cross-contamination. The function and significance of knowledgeable and experienced laboratory employees cannot be overemphasized [14].

Chest X-rays, microscopic inspection, the use of Gene-Xpert, and the culture of sputum or body fluids are all used in the diagnosis of active tuberculosis. The tuberculin skin test (TST) or blood tests are necessary for the diagnosis of latent TB [23, 15].

The lack of adequate gold standard complicates the estimation of sensitivity and specificity of TB diagnosis; therefore, there should be a frame work in place to evaluate the new and old methods for determining the presence of TB in subjects or patients.

SAMPLES

Obtaining the right sample play significant role in the diagnosis of TB; Specimens of sputum, stomach washings, and body fluids such as blood cultures, urine, feces, and cerebrospinal fluid could be used to isolate tubercle bacilli. All specimens must be gathered and sent in sterile, spotless, disposable, wide-mouthed, plastic, leak-proof, lab-approved containers that are not filled with fixative. Because mycobacteria are resilient, transport media or preservatives are typically not required [16].

For the recovery of AFB, swabs are not the best option [16]. Obtaining specimens before starting treatment is ideal. The inability to recover mycobacteria can make the diagnosis difficult, even after a few days of treatment[17]. As soon as feasible; specimens should be brought to the laboratory and kept cold until processing is completed. International law governs the movement of infectious materials, and laboratories must be complied with it.

CULTURE

According to [18], culture is the gold standard and most trustworthy method for diagnosing tuberculosis (TB), with detection limit of 101–102 viable organisms [4]. It is necessary in order to have isolates available for susceptibility testing, the findings of which are required in order to provide the patients with appropriate care. A case of tuberculosis (TB) that has been proven by culture is considered to be caused by the M. tuberculosis complex [19]. In genotyping studies, which are essential for epidemiological inquiries and monitoring laboratory cross-contamination, isolates are also required [20].

Since Mycobacterium TB grows slowly, it requires unique media and techniques that aren't needed for the growth of other organisms [21]. The "traditional" methods of culture, such as agar and egg-based media, Middle Brook broths, or solid media, have been replaced by the semi-automated Bactec 460 and, more recently, by continuous automated monitoring in liquid culture techniques (CAMLIC). There are two main media categories that are used frequently; Solid: made from eggs and agar, and liquid: also known as broth media.

MICROSCOPY

"Microscopic examination of stained smears is one of the ways of identifying the tubercle bacilli, for the presence of organisms that retain the primary stain when the smear is decolorized with an acid alcohol solution" is the definition of acid-fast bacilli microscopy where Ziehl-Neilson (ZN) staining method is used for the detection of TB. Ziehl-Nelson is superior to fluorescence staining of clinical material using auramine-o or auramine-rhodamine because ZN staining is more appropriate for determining the microscopic morphology of bacilli in positive TB cultures, but fluorescence staining is faster and easier to read.

Nucleic acid amplification tests (NAAT).

A revised algorithm from the CDC [22]provides useful guidelines for using nucleic acid amplification tests (NAAT) on material directly. In patients with signs and symptoms of pulmonary tuberculosis (TB) for whom a diagnosis of TB is being considered but not yet established, and for whom the test result would change case management or TB control activities like contact tracing, the Center for Disease Control and prevention (CDC) now recommends that NAAT be performed on at least one respiratory specimen [22].

PCR and Restriction Endonuclease Analysis.

To enable the quick identification of mycobacteria down to the species level, Telenti updated the Polymerase Chain Reaction (PCR)-Restriction Endonuclease Analysis approach in 1993. This modification became known as the participatory rural appraisal (PRA) method. The technique has been widely applied to the identification of mycobacteria. The main drawback is that it is not marketed, does not bear CE3F, and lacks US Food and Drug Administration (FDA) certification.

DNA SEQUENCING

Because mycobacteria grow slowly, having access to DNA sequencing technology is very helpful for identifying these organisms. Some clinical laboratories are now using DNA sequencing in a practical capacity, thanks to recent advancements in the automation of target amplification and sequence analysis [4]. The approach should only be used in reference laboratories due to its high equipment requirements.

EVALUATION OF NEW TESTS FOR TB INFECTION

In order to achieve the End TB Strategy, it has become imperative to evaluate the tests method used in the diagnosis of TB;this is because lack of an adequate gold standard complicates the determination of sensitivity and specificity, the standard approach to assess the performance of new diagnostic tests. Surrogate reference standards are therefore proposed. A hierarchy of reference standards was developed when WHO reviewed evidence on the use of interferon gamma release assay (IGRA)[23]. Reference standards at higher levels of hierarchy should provide stronger evidence for a tests accuracy to identify people who would benefit most from Tubercle Preventive Treatment. New tests for TB infection currently in the pipeline are based on similar concept to TST and IGRA; that is, eliciting an immune response to Mycobacterium tuberculosis specific antigens either in vivo (size of skin induration) or invitro(magnitude of cytokine release)[24].

TB TREATMENT, MANAGEMET, AND RESISTANCE.

The treatment of tuberculosis (TB) infection, also known as tuberculosis preventive treatment (TPT), is critical component needed to achieve the ambitious targets of the End TB Strategy2030-2035 [25]. Management of TB infection is also critical to pursue TB elimination [26]. Without the prospect that a new efficacious and safe TB vaccine can be developed and scaled up worldwide in the foreseeable future, continued measures to expand the provision of effective TPT remain of critical importance. Furthermore, at the first United Nations High-level Meeting on TB in 2018, member states committed to provide TPT to more than 30 million people in 2018-2022: 6 million people living with HIV (PLHIV), 4 million children aged <5 years who are household contacts of people with TB and 20 million other household contacts [27].

Progress in expanding TPT coverage among contacts of TB patients has been very limited up to now, with approximately half a million contacts in 2019 [28]. There is no gold standard method for diagnosing TB infection [29]. The World Health Organization (WHO) currently recommends a tuberculin skin test (TST) or an interferon- gamma release assay (IGRA) to test for TB infection [30].While governance is essential for organizing responses to global health emergencies like tuberculosis (TB), its contribution to improving TB control has not gotten much attention. Many low- and middle-income countries (LMICs) still struggle with tuberculosis, and Nigeria is one of the top three nations that account for 80% of the overall difference between reported cases and incidence in 2017. Nigeria is one of the 30 countries with the highest TB burden. WHO, (2018), [31,32, 33].

Historically, TBhas quickly evolved to be resistant to anti-TB drugs, resulting in increasingly resistant strains of TBarising over time. The original main drivers of resistance were low user adherence to treatment regimens, prescription of poor-quality drugs or drugs that didn't match the TB resistance profile, and prescription of the wrong dosage of antibiotics, [34]. These factors contributed to a setting in which TBbacteria were exposed to antibiotics at a level that allowed resistance mutations to accumulate but prevented complete clearance of the infection. Today, the incidence of Drug Resistant-TB is now largely driven by transmission of the resulting Drug Resistant-TB strains.[34].

The successful treatment of TB and Drug Resistant-TB relies on rapid detection and accurate drug resistance profiling. Traditional phenotypic drug susceptibility testing (DST) relies on the slow culture of TB bacteria, which requires several weeks of incubation in Biosafety Level 3 (BSL-3) laboratories [35]. Since many low-income regions lack access to BSL-3 laboratories and resources [36], culture-free molecular DST represents an attractive TB diagnostic alternative. However, available molecular assays are limited to detecting a restricted panel of specific mutations associated with resistance to only one or a few anti-TB drugs [35].

Since TB is continually adapting to new anti-TB drugs and evolving cognate resistance mutations, there is a need for a faster and more accurate method to distinguish drug-resistance properties. Next-generation sequencing (NGS) represents a rapid and precise platform for detecting and combatting Drug Resistant-TB.[35].

PREVENTION

The following are essential for the effective prevention, control, and eradication of tuberculosis (TB) in order to achieve End TB Strategy 2030-2035:

1. Administrative aspects: these include prompt surveillance and investigation, diagnosis, and treatment. The treatment of TB infection also known as tuberculosis preventive treatment (TPT) is a critical component needed to achieve the ambitious targets of the End TB Strategy2030-2035. WHO, 2015.

2. Since TBcontinues to develop new drug resistance mutations as new treatment regimens are implemented and repurposed, the need for early, rapid, and precise diagnostic testing to identify resistance is becoming increasingly critical. Accurate determination of the drug resistance profile of TB at both the individual and population levels can provide guidance for accurate treatment plans and community-based eradication programs, respectively.

3. Implementing standard precautions, which are a set of work practices that require all healthcare workers to assume that all blood, body fluids (except sweat), excretions, and secretions from all patients in all settings are potential sources of infection, is essential for the effective prevention and control of tuberculosis.

4. Describes the components of Airborne Precautions and how to use them in the treatment of an infectious tuberculosis case, whether it is suspected or confirmed.

5. BCG Immunization; immunization against TB should be encouraged. The population who testsnegative for TB should be given BCG immunization.

CURRENT CHALLENGESINTB MANAGEMENT AND CONTROL

The current challenges in the management, control, and eradication of TB includes the following:

- Missing cases due to improper diagnosis.
- Lack of adequate health care facilities for diagnosis.
- Lack of vaccine availability.
- Insecurity associated with some states in the zone.
- Knowledge gaps.
- TB co-infection with other related diseases e.g.HIV.
- Undetected latent TB carriers which serve as reservoirs for the spread of TB.
- Drug resistance cases in TB management.

CONCLUSION

The unaccounted-for TB cases continue to serve as a reservoir for new cases to arise in the area and spread the disease. The identification of missing TB cases will continue to be the top priority for TB control in Nigeria over the coming years, as one infectious TB case can infect roughly 15 to 20 people annually if left undetected and untreated. TB is still a serious illness that has an impact on public health in North Central Zone and Nigeria in particular.

Although the incidence of tuberculosis (TB) is high in the area, the rate of TB case identification and notification is low in comparison to the predicted number of TB incident cases that should be notified based on population. If the End TB strategy, of eradicating tuberculosis by 2030 - 2035 is to become a reality in the zone and throughout Nigeria, then TB program managers, partners, and the Federal Ministry of Health should design interventions based on the disease burden per state in the zone and in Nigeria as a whole.

RECOMMENDATION

The government, partners and the corporate sectors must collaborate in order to create awareness and educate the public about TB testing and to put structures and procedures in place to check for missing TB carriers, which act as a reservoir of transmission, if the End TB Strategy targets for 2030 and 2035 is to be achieved.

Breakthroughs in research, such as the development of a new vaccine, are necessary to quickly bring the global incidence of tuberculosis down to the levels which low-burden nations have already attained. Otherwise; in North Central Nigeria, there is little chance of achieving the End TB strategies of 2030 and 2035.

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