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Research Article

Drug Resistant Tuberculosis in Nigeria: A Case of Ondo State Patients

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Abstract

Tuberculosis (TB) remains a global public health problem, with developing countries bearing the highest burden. In the first and second quarters of 2021 in Ondo State 9,207 TB cases were reported, out of this figure 1106 cases were positive and 27 patients were drug resistant. The result of the visitation of patients to TB clinics in Ondo State was found successful in achieving its objectives; still there is concern of cases and defaulters. The aim of this study is to evaluate the directly observed treatment outcomes, patient deaths, treatment failures, and follow-up status of tuberculosis (TB) patients. This study was conducted on 27 TB patients put on treatment during the first and second quarters of 2021 Ondo State. The ages of the patients range between 10 and 59 years old. The majority of the patients were males, 59.25% (16) while female were 40.75% (11). 59.26% (16) has the highest height (cm), 13 (48.15%) has the highest weight of between 50-59kg. Out of total 27 TB cases obtained, 55.6% were cured, 22.2% follow-up (continued treatment), 18.5% died, and 3.7% failed. Defaulters were high in present study. The majority of patients left the treatment due to feeling well. The study present patterns of DR-TB in Ondo State, Nigeria. Ondo State has a high prevalence of TB, including resistant TB and there is the need to increase monitoring of individuals resident in this region. Efforts should be geared to providing more free services to the patients and more should be done to avoid patients from being stigmatized.

Keywords: Tuberculosis, TB burden in Ondo State, Treatment Outcome, Follow-up

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Introduction

With an estimated 4700 patients suffering from drug-resistant tuberculosis (DR-TB) in 2015, Nigeria has the second-highest TB burden in Africa and is one of the 30 countries with the highest DR-TB burden. Only 1241 of these DR-TB patients were found, and 656 of them were given treatment in Nigeria (WHO, 2016). With increased use of the GeneXpert® MTB/RIF technology, which enables the rapid diagnosis of rifampicin-resistant TB, the treatment gap for DR-TB patients still exists and may even be widening. Policymakers and practitioners are being urged by this quickly changing environment to improve and scale up the delivery of DR-TB treatment.

Every year on March 24, World TB Day provides an opportunity to increase public awareness of the prevalence of tuberculosis (TB) worldwide and the state of TB prevention and care initiatives. In order to advance efforts to end TB, it is also an opportunity to mobilize political and social commitment. Overtaking HIV/AIDS as the top infectious cause of death globally, TB is the ninth leading cause of death overall. The African region accounts for more than 25% of TB deaths. Multidrug-resistant tuberculosis (MDR-TB) has the potential to jeopardize advancements made in the fight against the disease. In order to fulfill the promise of providing high-quality TB prevention and care services to everyone, as well as enabling TB prevention through multi-sectoral development efforts, World TB Day offers a platform for affected individuals and communities, civil society organizations, health care providers, policy makers, development partners, and others to advocate, discuss, and plan future collaboration.

The Ondo State reported a total of 1,106 cases of tuberculosis between January and June 2021, according to the National Tuberculosis and Leprosy Control Program (NTBLCP). The cases were documented across the state's 18 Local Government Areas, according to the state coordinator of the program (Johnson, 2021). The coordinator said the fight against tuberculosis was still going on as the nation struggled to contain the COVID-19 pandemic, who spoke in Akure, the state capital. In his statement, he made note of the agency's nationwide campaigning efforts and noted that cases were reported on a quarterly basis. He described the breakdown of the cases, stating that 471 cases were recorded from April to June, compared to 635 cases from January to March. According to the report at our national headquarters, 635 cases of tuberculosis were found and reported in Ondo State's 18 Local Government Areas during the second quarter of 2021, or from April to June 2021.

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Statement of the Problem

Tuberculosis (TB) remains a global public health problem and one of the top ten leading causes of death, worldwide, with developing countries bearing the highest burden (WHO, 2020). In 2018, Nigeria was listed as first in Africa and sixth among the 30 countries of the world with the highest TB burden (WHO, 2020). Unfortunately, the problem of TB in Nigeria has been complicated by the emergence and spread of drug resistant TB and a high burden of HIV/AIDS (NTBLCP, 2017; WHO, 2018). The problem of TB is worsened when there is also a high burden of HIV infections, as people with HIV are more likely to develop active TB. According to WHO reports, an estimated 63,000 Nigerians living with HIV/AIDS develop TB, while about 39,000 die from the disease, each year (WHO, 2018). To further compound the problem, Nigeria is ranked among the 10 countries that accounted for 77% of the global gap in TB case detection and notification in 2016. It is reported that Nigeria contributes about 8% of the 4.3 million TB cases missed globally. Consequently, in 2019, WHO initiated 'community-informant' methods to find missing TB cases in Nigerian communities (WHO, 2019). The initiative covered 12 high burden states in Nigeria, but Ondo State was not part of the study. However, according to data gathered from Ondo State Ministry of Health, Ondo State has a notification gap of more than 9,207 TB cases in the first and second quarters of 2021.

Literature Review

Drug resistance is a biological phenomenon that has been observed in *Mycobacterium tuberculosis* since the discovery of the first anti-TB drug, streptomycin. Many patients who were injected with streptomycin were brought from the brink of death and their sputum became temporarily clear of *M. tuberculosis*. But despite continuing to receive treatment, they soon began to excrete bacilli that were resistant to streptomycin in the laboratory (Pyle, 1947). With the advent of new drugs, thioacetazone and para-aminosalicylic acid in 1948 and isoniazid in 1952 it became clear that combination chemotherapy was the key to preventing the development of resistance. Initial combination regimens required 18 months of treatment, but the invention of rifampicin in 1957, the most powerfully sterilizing anti-TB drug, paved the way for development of the shorter and more effective isoniazid- and rifampicin-containing regimens known as short-course chemotherapy (Kwonjune *et al.*, 2015). Rifampicin, isoniazid, Pyrazinamide and Ethambutol are the commonly recommended regimen for the treatment of TB for 6 or 9 month called RIPE. As part of the global TB control strategy called DOTS (directly observed treatment, short-course), these regimens became the standard of care even in resource-limited settings starting in 1993. The continuing spread of drug-resistant tuberculosis (TB) is one of the most urgent and difficult challenges facing global TB control. Patients who are infected with strains resistant to isoniazid and rifampicin, called multidrug-resistant (MDR) TB, are practically incurable by standard first-line treatment (Kwonjune *et al.,* 2015).

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Even though tuberculosis (TB) is a treatable infectious disease, an estimated 1.3 million people died from TB in 2012 as a result of evolve resistance to drugs (WHO 2013a). For patients with drug-susceptible TB, standard treatment based on isoniazid and rifampicin, the two most powerful drugs, results in excellent cure rates. Patients who are infected with strains resistant to isoniazid and rifampicin, called multidrug-resistant (MDR) TB, are practically incurable by standard first-line treatment (Kwonjune *et al.,* 2015).

Drug resistant tuberculosis poses a major hurdle to achieving the WHO End TB Strategy targets. Acting early and decisively will be a determining factor in either future success or failure. Encouragingly, the past 5 years have seen new diagnostic technologies and treatment options become available, as well as strong global political commitment to end tuberculosis. Despite the obstacles threatening the realization of the WHO End TB Strategy targets in Africa, there are equally effective tools available for achieving success (Gbadebo *et al.,* 2020).

Ensuring routine standardized algorithms detecting rifampicin and second-line resistance is the ideal and should be facilitated in the era of the Xpert MTB/RIF and GenoType MTBDR*sl*. A few countries have shown high uptake of rapid diagnostic tools for early rifampicin and second-line resistance detection.

HIV Co-infection with tuberculosis

Bacteria become active as a result of anything that can reduce the person's immunity, such as HIV, advancing age, diabetes or other immune-compromising illnesses. People living with HIV are vulnerable to MDR-TB infection and are at high risk of developing active MDR-TB once infected. TB strains are often less fit and less transmissible, and outbreaks occur more readily in people with weakened immune systems like patients with HIV (Fischl *et al.,*1992). HIV-positive patients often die while waiting for laboratory confirmation of MDR-TB and before starting effective therapy. This was best illustrated by the rapid and deadly spread of XDR-TB among HIV-positive patients in South Africa (Gandhi *et al.,* 2006). WHO currently recommends Xpert MTB/RIF as the initial diagnostic test in settings with high prevalence of HIV-associated TB or MDR-TB (WHO 2011b). Co-morbidity of HIV within prison populations has also been shown to worsen health outcomes. Nachega articulate that while HIV-infected prisoners are not more susceptible MDR-TB infection, they are more likely to progress to serious clinical illness if infected *(*Nachega, 2003).

Ending tuberculosis and specifically drug resistant tuberculosis cannot be fully realized without dealing with HIV infection and disease. HIV/AIDS is a major contributor to the burden of both tuberculosis and drug resistant tuberculosis**.**

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How does drug resistance happen?

Antibiotic resistance was first identified by scientists in the1940s. The Centre for Disease Control and Prevention (CDC) has since then declared antibiotic resistance one of the "most urgent public health problems" worldwide as a result of more antibiotic-resistant infections that have developed. Resistance in Mycobacterium TB thought to be due to the low permeability of the cell envelope and the numerous efflux pumps encoded in the MTB genome, this arises through mutation. Resistance to anti-TB drugs usually occur when prescribed drugs are used wrongly. This could happen when patient fails to complete their full course of treatment probably due to health-care providers prescribing wrong treatment, poor quality drugs or wrong dose. Patients might stop treatment prematurely as a result of non-availability of drugs at the appropriate time. First-line treatment could failed as well and the condition of the patient not improving. Despite this, it is still very possible to treat drug-resistant TB but most likely not to be able to take the first-line medication.

Before treatment of MDRT can be embanked on details history of the past TB treatment must be known, especially Patients who had received first or second line of anti TB drugs. Any regime already taken that is not cure are most likely not to be effective again even if it is susceptible using Direct Sensitivity Testing, DST.

Risk factors for MDR-TB

Following factors are associated with the risk in multi-drug resistant tuberculosis (Kwonjune *et al.,* 2015).

- Failure to respond to a first-line DOTS regimen (WHO Category I or II)
- Relapse after a full course of treatment with a first-line regimen
- Treatment after defaulting from treatment with a first-line regimen
- Exposure to a known case of MDR-TB
- Exposure to TB in institutions with high prevalence of MDR-TB, such as a prison or hospital
- Living in areas or countries with high prevalence of MDR-TB
- Persons suffering from conditions that impair the immune system such as HIV

Objective of Study

This is a preliminary case study. In the first and second quarters of 2021, this study was designed to evaluate the drug-resistant tuberculosis (DR-TB) prevalence in Ondo State. The purpose of this study is to evaluate the directly observed treatment outcomes, patient deaths, treatment failures, and follow-up status of tuberculosis (TB) patients.

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Theoretical Framework

To help inform the creation of interventions and better understand the challenges to TB evaluation, a series of qualitative interviews have been carried out (Cattamanchi, *et al.*, 2015). The Theory of Planned Behavior has served as the framework for this procedure. A systematic review of studies on the implementation of guidelines revealed that the Theory of Planned Behavior was the theory that most accurately predicted adherence to recommendations (Godin *et al.*, 2008). This theory contends that behavior can best be predicted by intention, and that the strength of intention is mediated by three variables: attitudes (the expected value of behavioral performance), subjective norms (what others think about the behavior), and self-efficacy (the belief that one can overcome obstacles to behavioral performance) (Ajzen, 1985).

Materials and Methods

Study area

The study was conducted in Ondo State, Nigeria. The metro area population of Ondo State in 2021 was 691,000, a 3.75% increase from 2020. The metro area population of Ondo State in 2020 was 666,000, a 3.74% increase from 2019 (United Nations, accessed 2022). The state is characterized by low socio-economic indicator, with a majority of the residents engaging in low-income generating activities, such as small trading and peasant farming.

Study population

Twenty-seven patients of various ages who volunteered to take part in the study and were visiting the clinic at the State Public Health Centers, General and Teaching Hospital in the Local Government Areas, Ondo State with a productive cough or a presumed diagnosis of tuberculosis made up the study group. People who clinically or symptomatically tested positive for tuberculosis and those younger than 19 years old were not included in the study.

Statistical Analysis

The data received was subjected to statistical analysis using Excel 2013 and Minitab 16 software.

Results and Discussion

Figure 1 depicts the number of TB cases, positive, and DR-TB cases in Ondo State. In the first and second quarters of 2021 in Ondo State 9,207 TB cases were reported, out of this figure 1106 cases were positive and 27 patients were drug resistant. The prevalence rate of positive TB cases and DR-TB cases are in the range of 12.01% and 0.29% respectively.

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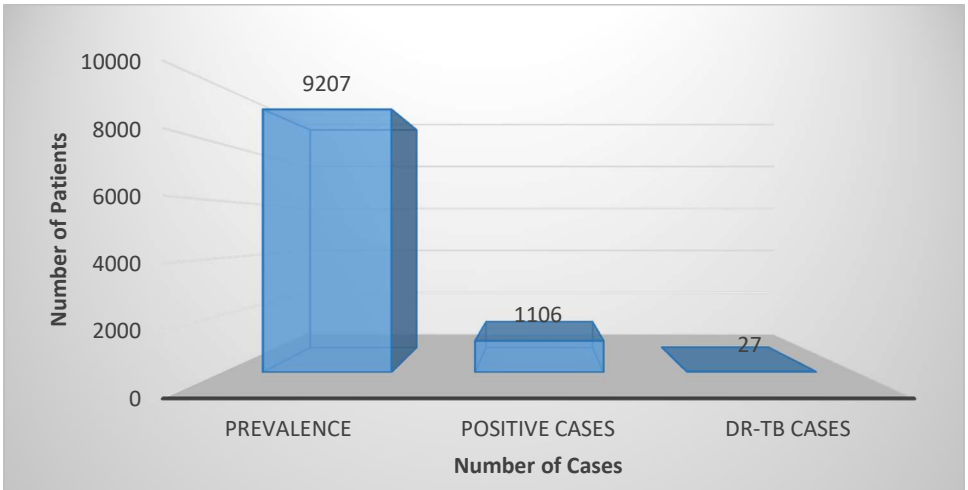

Figure 1: Number of TB Cases in Ondo State

The demographic characteristics (age) of the 27 study patients with DR-TB are shown in Figure 2. The range was from 19 to 59years, eight patients were in the range of 20 and 29, while another 8 was between 40 and 49. The least age range was 10-19.

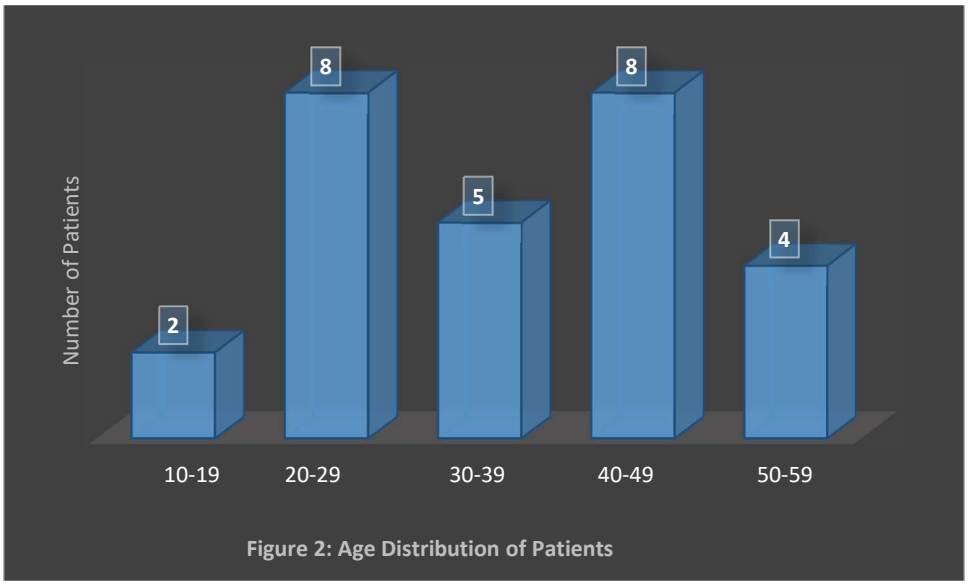

Figure 2: Age Distribution of Patients

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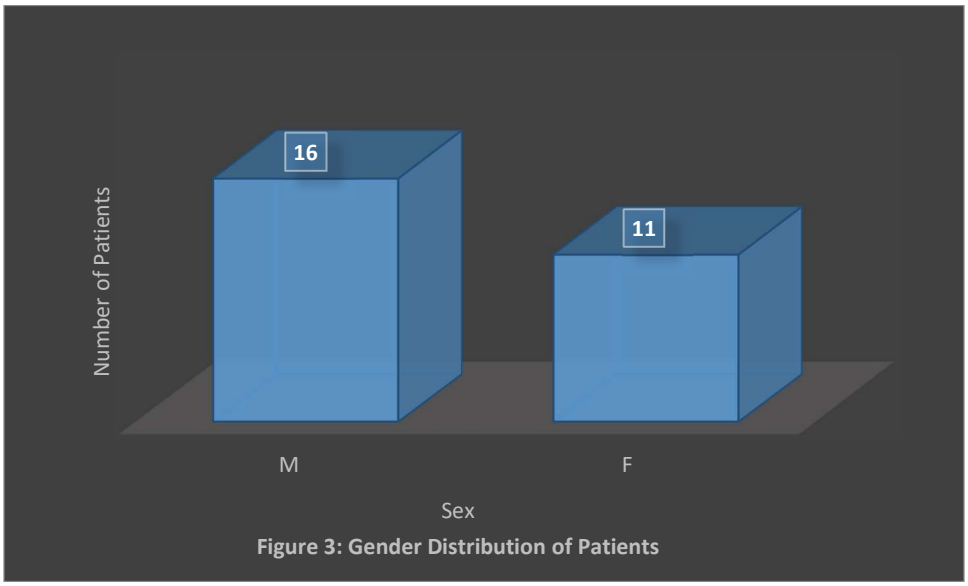

Figure 3: Gender Distribution of Patients

The gender distributions of patients in Figure 3 show that there were more males – 16 translating to 59.26% than females – 11 (40.74%). Of the 27 patients used in this study, majority of patients were men and information gave that they came from main town.

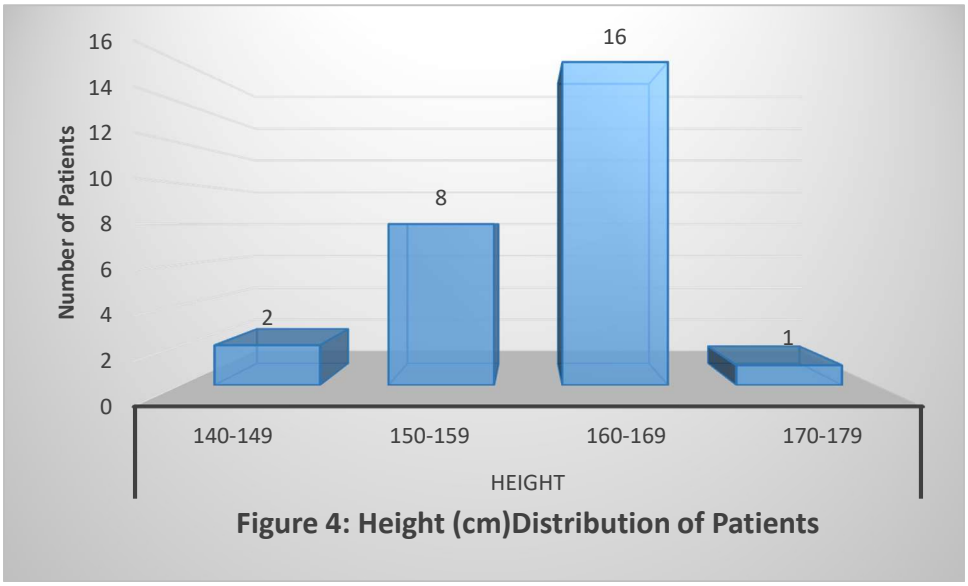

Figure 4: Height (cm)Distribution of Patients

Figure 4 displays the patients' distribution of heights. The height was between 140 and 179 centimeters. According to the graph, the range of 160–169 was the highest, followed by 150–159, 140–149, and 170-179 as the lowest. The study further showed that of the 140-

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149 range, two were females; there were two men and two females in the 150-159 categories. Men took the bulk of category 160-169 with 12 in number, while female **was** nine.

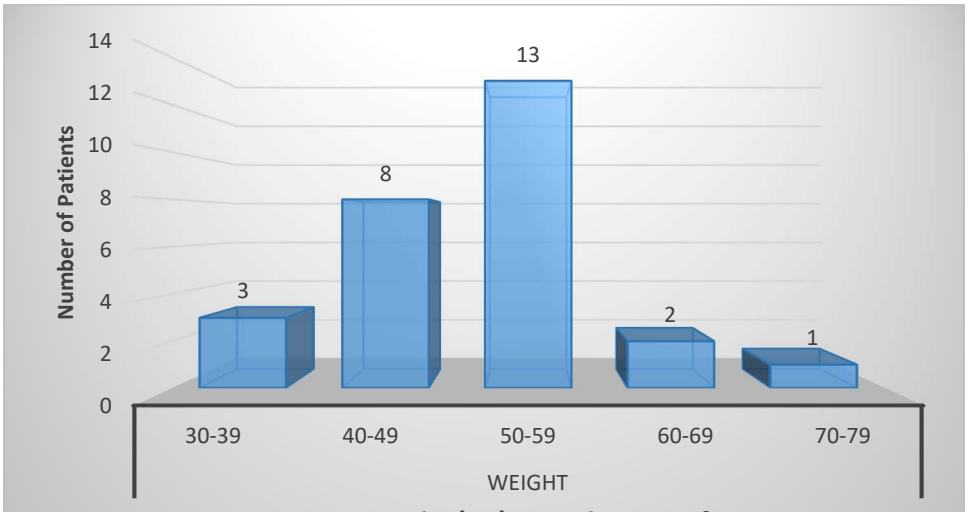

Figure 5: Weight (Kg) Distribution of Patients

The patients' weights were distributed as follows: 30-39 >40-49 >50-59 >60-69 > 70-79 Kg. The only heaviest patient was a female (75.4kg), but the highest number of patients was thirteen at weight range of 50-59 kg depicting eight male and five females. There were four each of male and female at the 40-49 kg range (Figure 5).

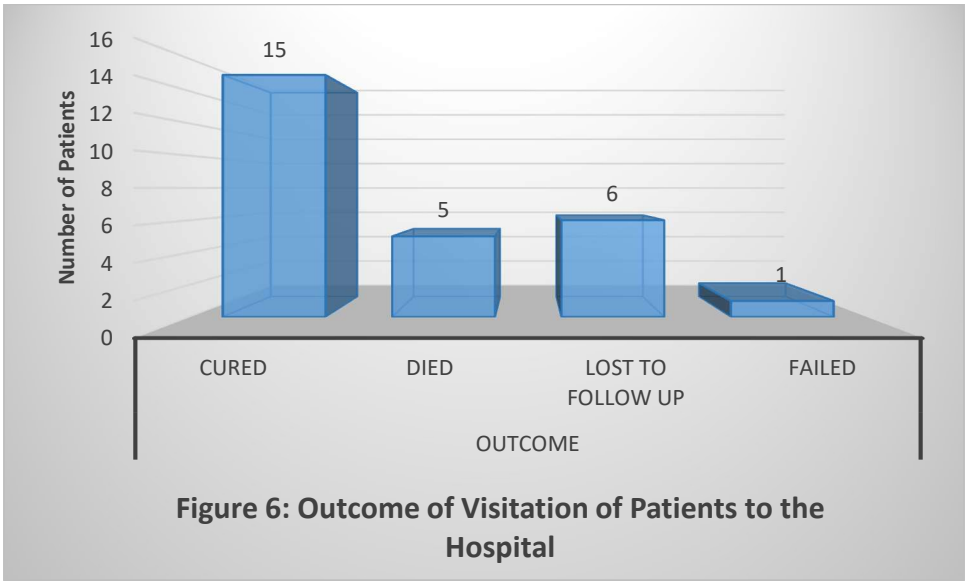

Figure 6: Outcome of Visitation of Patients to the Hospital

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Figure 6 displays the results of the patients' visits to the hospital clinic. According to the findings, of the 27 patients that visited the clinic, 15 or 55% were cured, 22% were lost to follow-up, 18.52% passed away, and 3.7% died. This suggests that the treatment given to the patients was effective. Out of the five that died, only one was female, and then three male patients were lost due to follow-up.

Discussion

From the results of the study, it is shown that there is high prevalence of TB cases in Ondo State, the reason could be due to the fact that people are more likely to: live and work in poorly ventilated and overcrowded conditions, which provide ideal conditions for TB bacteria to spread. According to Horton *et al.,* (2016), *men have a higher prevalence of TB and, in many settings, remain infectious in the community for a longer period of time than women*. Age-related immune senescence influences the presentation of tuberculosis (TB) in older patients (Aula *et al.,* 2019). Gender differentials in tuberculosis (TB) have been reported worldwide. Men are more likely to be diagnosed with TB than women, with a male-to-female ratio of 1.6:1, globally (WHO 2016; Marçôa *et al.,* 2018).The average age of the patients was 33.28 years.

As shown in Figure3, with comparison with the works of Oladimeji *et al.,* (2022), there was no statistically significant association with sex and age. According to Marçôa *et al.,* (2018), men have alcohol, drug, and smoking abuse than women; all these are the contributing factors for TB prevalence. TB prevalence is significantly higher among men than women in low- and middle-income countries, with strong evidence that men are disadvantaged in seeking and/or accessing TB care in many settings (Horton *et al.,* 2016).

The findings of Lonnroth *et al.,* (2009) revealed that body mass index (BMI) is an excellent predictor of relative TB risk, but they did not provide any additional information on the mechanisms through which nutritional status affects risk of TB. It may be questioned if BMI can be utilized as a causal factor in and of itself, which can be used to estimate the population-attributable proportion and to model the impact of population nutritional status on future TB incidence trends. This is because BMI is a crude indicator of nutritional status. Given this, the height of a patient may have an impact on the prevalence of TB. Studies indicate that being overweight and being tall are protective factors against TB. Low weight and height are known risk factors for the disease. Additionally, Lydia *et al.* (1971) demonstrated the link between body build and TB, Morbidity height- and weight-related increases and decreases.

According to a study, the type of TB was a determining factor for weight gain, with pulmonary TB patients having a five-fold higher risk of weight gain than extra

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pulmonary TB patients. Weight is utilized as a gauge of a TB patient's health. The majority of people who with MDR-TB are chronically unwell and undernourished (Franke *et al.*, 2008; Van Deun *et al.*, 2010). Gaining weight could be a valuable indication of therapy response for MDR-TB. It is simple, affordable, and convenient to measure weight increase. Weight loss is a common symptom in patients with TB. Treatment failure has been linked to weight loss during TB treatment. Inadequate dietary intake may confuse the impact of TB medication on weight (Gler *et al.*, 2013).

In the best treatment programs, (Mitnick *et al.* 2003., Shin *et al.* 2006 have reported cure rates of 60%–80%. which corroborates with this study. Globally, however, the cure rate for MDR-TB is much lower. In 2013, the WHO reported that only 48% of MDR-TB patients were cured.

This study's findings (Figure 5) are consistent with the positive MDR-TB results from Gler *et al.* (2013) in the Philippines, Rohini *et al.* (2013) in Chennai, India, and Cattamanchi *et al.* (2015) in (Uganda).

Conclusion

Drug-resistant tuberculosis (DR-TB) affects a large number of people worldwide, and Nigeria is not an exception to the TB burden in Africa. It is one of the 30 nations with the greatest prevalence of DR-TB. The case of Ondo State, Nigeria, is used in this study. The study's findings were based on information gathered at the TB facility headquarters in Akure. According to the study, out of the 27 TB cases for which data were collected, 55.6 percent were cured, 22.2 percent underwent follow-up therapy, 18 percent passed away, and 3 percent failed. The study's findings corroborate those of other nations' positive MDR-TB test results. This may indicate that the patients are receiving effective care. To minimize victims dying and abandoning treatments, it is advised that good counseling be implemented, treatment costs be made as avoidable as possible, and stigmatization be avoided.

Recommendations

- TB is one of the vaccine-preventable diseases which is also curable. The Bacille Calmette-Guérin (BCG) vaccine to be given at birth to help prevent serious TB infections in children.
- Community-based programs can improve treatment outcomes by allowing patients to be treated even in their homes and addressing socioeconomic barriers to adherence.
- Patients must stick to treatment plan by taking full course of treatment religiously.
- Appeal for continuous release of funds to cater for the infected patients

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- Frequent cancelling and appeal by health providers on how to take prescribed regime.
- Health provider should ensure prompt diagnosis, following recommended treatment guidelines, monitoring patients' response to treatment, and making sure therapy is completed.
- Proper antibiotics regimen must be prescribed at all times to prevent resistance development.

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