



## **Drug Resistant Tuberculosis in Oyo State, Nigeria: A Retrospective Study**

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### **Author's contribution**

*The sole author designed, analysed, interpreted and prepared the manuscript.*

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### **ABSTRACT**

**Aim:** The focus of this work was to evaluate the prevalence of rifampicin resistant tuberculosis in Oyo State, Nigeria.

**Study Design:** A cross sectional retrospective study

**Place and Duration of Study:** St Mary's Catholic Hospital, Ibadan, Nigeria, between October 2016 and March 2018

**Methodology:** In this study, 1044 patients diagnosed in the GeneXpert laboratory was conducted using the laboratory register. The age, gender, HIV Status, MTB analysis results and resistance to rifampicin were collected and analyzed.

**Results:** Of the 1044 tested, 177 (17%) tested positive for TB while 19 (10.7%) of the 177 were resistant to rifampicin. Fourteen (73.7%) of the 19 were male and 5 (26.3%) were female. Fourteen (73.7%) of the 19 fell between 21 - 40 years of age. Seven (36.8%) of the 19 resistant to rifampicin were HIV positive. Of the total 1044 patients tested, 601 (57.6%) were females and 443 (44.4%) were male.

**Conclusion:** This study showed that rifampicin resistant tuberculosis is high in Nigeria especially among the economically productive age group in the country. More attention should be committed to quick accessibility of diagnosis, treatment and monitoring by the policymakers.

**Keywords:** Rifampicin; drug resistant; tuberculosis; Nigeria.

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## 1. INTRODUCTION

The aetiologic agent responsible for tuberculosis infection is *Mycobacterium tuberculosis* (MTB). This bacterium majorly affects the human lungs, a condition referred to as pulmonary tuberculosis. However, this bacterium can as well spread to other organs of the human body and this is called extrapulmonary tuberculosis [1]. The transmission of this infection happens when victims of this disease cough, sneeze or spit. About 1.7 billion people worldwide are suffering from this infection but only five to fifteen percent of these people end up having TB disease in their entire life [1]. In 2014, approximately 9.6 million people were infected with TB worldwide according to World Health Organization with about 95% of them in the third world countries. Nigeria came third, after India and Indonesia in the list of the top 22 countries with high burden of tuberculosis [2].

Common predisposing factors to tuberculosis infection are smoking, alcohol consumption, diabetes, overcrowding and poor nutrition. People living with HIV (PLHIV) are highly at risk of the infection [2]. Studies have shown that the commonest opportunistic infection among people living with HIV is tuberculosis. Among PLHIV, 50 – 80% have been reported in sub-Saharan Africa to have TB co-infection [3].

About 100 years ago, bacilli Calmette-Guérin (BCG) vaccine was produced. The vaccine is still widely used and has prevented, in children, serious grades of TB [1]. The fight against *Mycobacterium tuberculosis* also recorded some success in the 1940s with the development of the first effective drug treatment against TB. However, there is presently no vaccine effective against TB infection among the grown-ups, either prior or sequel to TB infection exposure [4] and some strains of the bacterium are resistant to rifampicin and isoniazid, a case described as multi drug resistant TB (MDR TB). About 480, 000 new cases of multidrug resistant TB (MDR TB) were recorded globally in the year 2014 alone [1]. These multi resistant cases pose a serious health concern, particularly in developing countries where there is high endemicity with treatment related difficulties [1,2]. The resistance of *Mycobacterium tuberculosis* to rifampicin and other drugs makes treatment more exorbitant, elongated and often necessitate more toxic medications [5].

Molecular diagnosis of tuberculosis is fast gaining acceptance in many nations of the world

while smear microscopy is gradually being phased out (even though culture and microscopy are still important in monitoring treatment) [1]. The current WHO recommended rapid diagnostic assay is Xpert MTB/RIF (Cepheid, USA). It was at first recommended for diagnosis among adults in 2010 but later extended to diagnose children and certain types of extrapulmonary tuberculosis in 2013 [1]. It works on the principle of real time polymerase chain reaction. It recognizes the MTB DNA in the sputum sample and detects the mutated gene responsible for resistance to rifampicin [6,7]. This diagnostic technique is more sensitive and specific than smear microscopy. It generates results in less than two hours.

In spite of this and other various advancements in TB diagnosis, a number of TB cases are still diagnosed clinically instead of laboratory confirmation. More than 40% of cases reported to WHO in the year 2016 were not confirmed in the laboratory [1]. The focus of this work was therefore to evaluate the prevalence rate of rifampicin resistant tuberculosis in southwest Nigeria and to point out the need for more commitment in the fight against this menace especially by our policymakers.

## 2. MATERIALS AND METHODS

### 2.1 Study Area

This work was performed in the GeneXpert laboratory of St Mary's Catholic General Hospital, Ibadan. This hospital receives patients from within the state and it is a referral laboratory to adjoining health facilities (both private and government).

National Agency for the Control of AIDS (NACA) established the GeneXpert laboratory in 2016 for quick diagnosis of TB with technical support from APIN Public Health Initiatives.

### 2.2 Study Participants

A cross sectional retrospective study of 1044 patients who were diagnosed in the GeneXpert laboratory between October 2016 and March 2018 was done using the laboratory registers.

The study participants were those with suspected pulmonary tuberculosis who visited the DOTS Centre and the HIV Clinic of the hospital and samples from other neighboring health facilities (such as Adeoyo Maternity Teaching Hospital,

OLA Oluyoro Catholic Hospital, Agbongbon PHC, Olomi PHC among others). The demographic characteristics of the patients extracted were: gender, age, HIV Status, MTB results and susceptibility or resistance to rifampicin.

### 2.3 Inclusion and Exclusion Criteria

Inclusion criteria were appropriate pulmonary sample, complete data, and definite MTB results while extrapulmonary and inappropriate sample, incomplete data, and indeterminate MTB result were the exclusion criteria.

### 2.4 Sample Processing

Preparation and processing of the samples were done following the national guideline on GeneXpert MTB/RIF assay. Sputum samples of between 1 and 4 mls were collected and checked for the presence of blood or food particles. Suitable samples were digested and decontaminated with sample reagent (SR) in a ratio of 1:2. Twice in fifteen minutes, the content was manually agitated for adequate digestion.

Two milliliters (2mls) of the homogenized sample was pipetted into the cartridge which was then uploaded into the GeneXpert machine. The result was self generated by the machine after approximately two hours.

### 2.5 Data Analysis

Analysis was done using the descriptive statistics (percentages, mean, and standard deviation), ratio and Chi-square tests and the significance of

tests was decided at  $P = 0.05$ . The results have been demonstrated with tables and graphs.

## 3. RESULTS

This work showed that of the 1044 screened for TB, 177 tested positive for TB putting the prevalence of pulmonary tuberculosis in Ibadan, Southwest Nigeria to be 17% (Fig. 1). 19 (10.7%) of the 177 were resistant to rifampicin. This study further demonstrated that the male gender have more cases of pulmonary tuberculosis with 22.1% (98/443) than the female gender with 13.1% (79/601). The same trend was observed with rifampicin resistant tuberculosis. The male gender had the higher cases of rifampicin resistant tuberculosis with 3.2% (14/443) while the female gender had 0.8% (5/601). Of the total patients tested, 601 (57.6%) were females and 443 (44.4%) were male. Nineteen (1.8%) of the 1044 overall study participants were found resistant to rifampicin.

This study, as shown in Fig. 2, depicted that of the 177 TB positive cases, 70 (39.5%) were HIV positive and 107 (60.5%) were HIV negative. There was a female gender preponderance of 51.9% (41/79) while the male had 29.6% (29/98).

According to Fig. 3, 49.8% (520/1044) of the study population were HIV positive out of which 12.1% (63/520) of those positive to HIV had a co-infection with tuberculosis. 7 (1.3%) of the 520 HIV infected group had a co-infection with rifampicin resistant tuberculosis. 19.3% (95/493) of those negative to HIV were positive to tuberculosis while 2.4% (12/493) of the HIV negative group were found resistant to rifampicin. Of the overall 1044 study participants, 19 (1.8%) were found with rifampicin resistant tuberculosis.

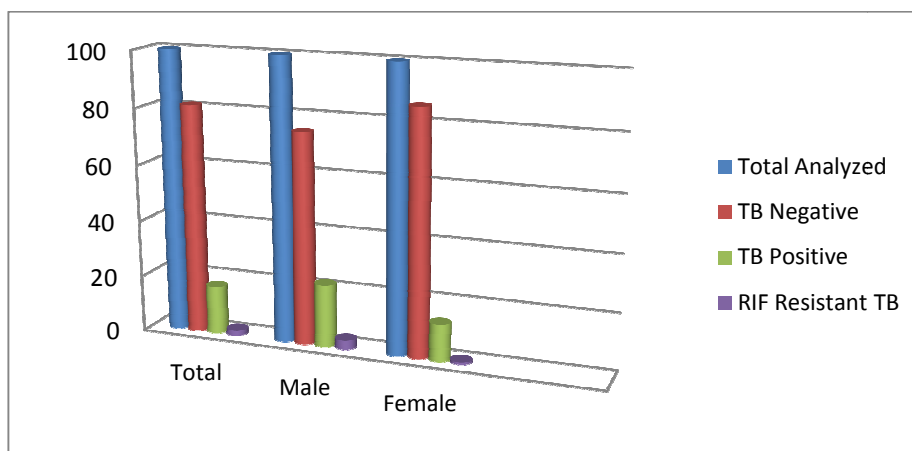
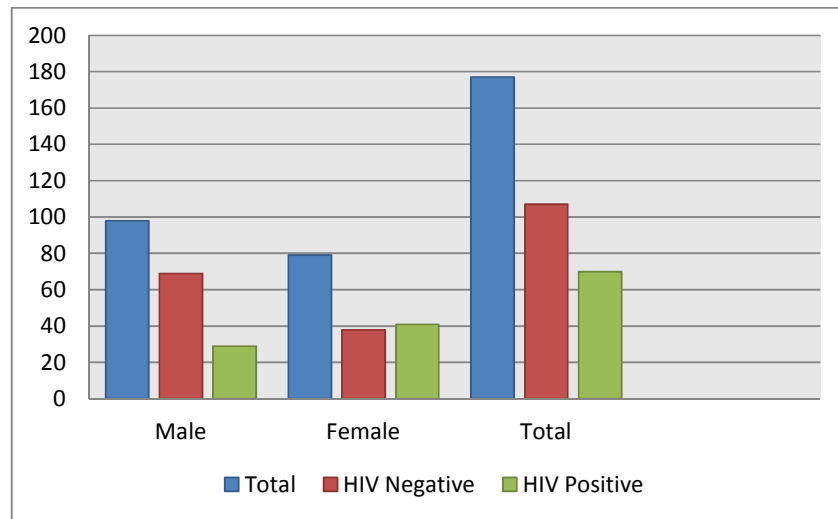


Fig. 1. RIF Resistant TB distribution according to gender in Ibadan



**Fig. 2. Pulmonary TB distribution among HIV Infected patients according to gender**

Fig. 4 shows that the most affected age group for TB is 31 – 40 years (42.9%) for both male and female keenly followed by age group 21 – 30 (21.5%) for both male and female. The same age groups also have the highest number of HIV cases respectively in both genders. Both age groups have equal number of male rifampicin resistant TB cases. Age group 21–30 had 71.4% while 31-40 had 57.1%. The highest burden of co-infection of rifampicin resistant TB and HIV was observed among 31-40 age group with 60% male and 40% female.

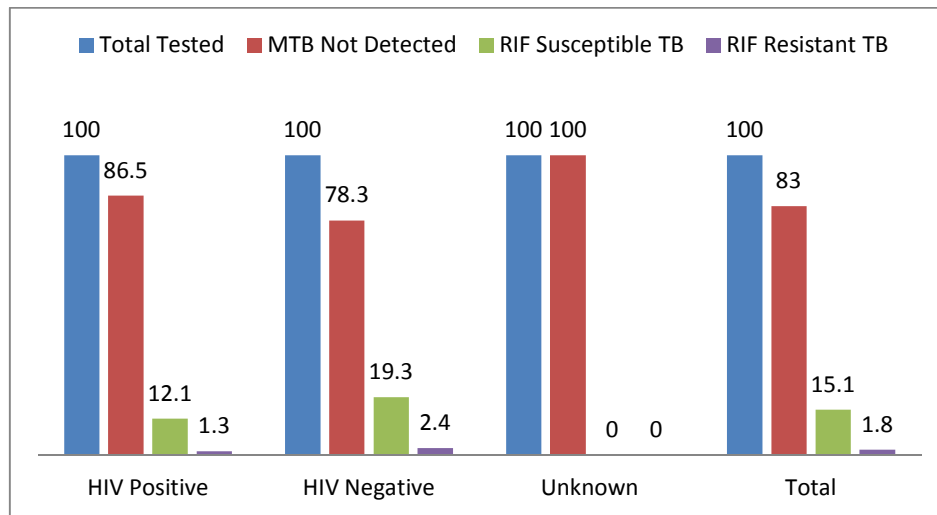
#### 4. DISCUSSION

This study revealed the prevalence of rifampicin resistant tuberculosis cases to be 10.7%.

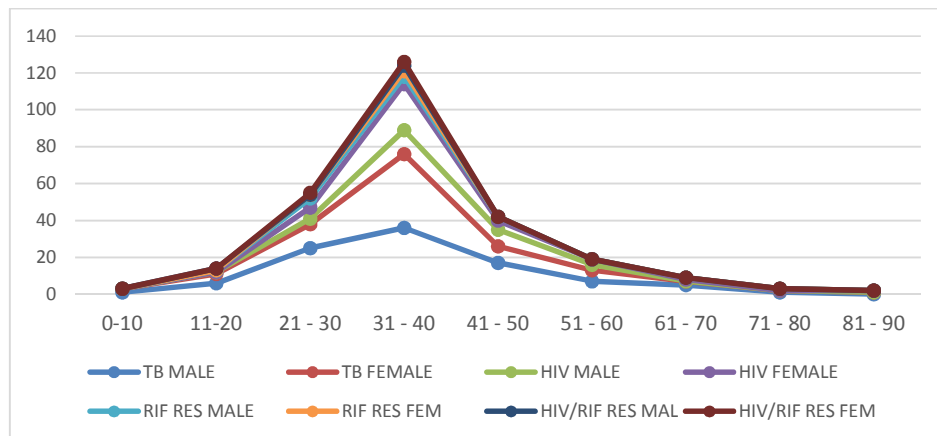
The findings of this research is similar to 7.2% and 12.1% rifampicin resistant TB prevalent rate gotten in Kwara and Nasarawa states by Rasaki et al. [8] and Audu et al. [9] respectively among the same study population. It is also in agreement with 12% reported by Adetunji et al. [10] among PLHIV. Other authors have reported similarly high prevalence rate in the country ranging from 7.1% to 18.8%. [11-13]. This current report is also in conformity with 2017 WHO report of 11% in Nigeria. [14]. It is however at variance with 19% report from Lawson et al. [15] and Idigbe et al. [16] with a 2% record in Lagos State but different from the findings of Otu et al. [17] who reported no rifampicin resistant strain. Adetunji et al. [18] reported 25.7% in an earlier work among the same study population.

The rates of prevalence varied from one part of the world to the other. The rate of resistance to rifampicin in South Africa was reported to be between 7.3 – 10% while 20.5 - 22% was reported in Indonesia. [2,19,20] Estonia and Uruguay reported 36.9% and 1.7% respectively. [3] These results demonstrate the ugly but rapidly increasing rate of resistance to rifampicin and the serious necessity of adhering to the correct management of TB in a bid to prevent the occurrence of drug resistance. Factors influencing drug resistance could be from the patients or the managing clinicians. When a patient fails to strictly follow instructions given on the appropriate usage of drugs, resistance is most likely to set in. On the other hand, clinicians have their share, as poor prescription practice, dosage, length of treatment coupled with non conformance to national algorithm on TB management could be responsible for drug resistance. Drug resistance can also be due to genetic mutations.

The 17% pulmonary tuberculosis prevalence rate reported in this work is lower than the 23% and 25.5% both reported in Nigeria's Northern region by Aliyu et al. [21] and Sani et al. [22] respectively in their independent studies. The report of this study is however greater than the 6.9% prevalence rate earlier reported in Ibadan by Kehinde and Okesola [23]. The fact that this current study was performed in a hospital which happened to be a referral centre to adjoining health facilities could probably account for the high prevalence rate compared to earlier works in the city. The major drivers of tuberculosis



**Fig. 3. Rifampicin resistant TB cases according to HIV status**



**Fig. 4. Age groups and gender distribution among TB, HIV, TB/HIV, RIF resistant TB and HIV/RIF resistant TB cases**

especially in the developing countries like Nigeria are poverty, poor nutrition, overcrowding and no or limited access to quality health care services. [24].

Rifampicin resistant tuberculosis was found higher among male than female (ratio 4:1 male to female). The report of 73.7% male preponderance in this study aligns with the 60% and 61.5% documented by Rasaki et al. [8] and Taura et al. [25] It further aligns with previous studies in the country [19,20]. Similar studies from other nations also confirm results of this current work that the development of resistance to rifampicin has a close connection with male than female [17,20]. This may not be unconnected to the fact that the predisposing

factors are commoner in male gender such as overcrowding, high adventurous moves like smoking etc, more daily outward activities to make ends meet and comparatively poor personal hygiene among men.

Age group 21 - 40 years had the highest prevalence of rifampicin resistance cases in this work with 36.8%. This is in harmony with the WHO report of 25 to 54 age brackets [1]. Audu et al. [9] found in their study that more than eighty percent of their study participants who were both *Mycobacterium Tuberculosis* and drug resistant TB positive fell between 11 – 40 years of age. This age range corresponds with the age most at risk for HIV infection, with high prevalence of coinfection with TB. This was however different

from reports by Imam and Oyeyi [26] who documented age group 15 - 29 years. This shows that rifampicin resistant TB is no respecter of age.

This study showed that 36.8% (7/19) of the rifampicin resistant patients were people living with HIV, 71.4% of which were between age 31 and 40. This could be a result of the socioeconomic pressure on people of this age range to cope with life and make a meaning out of it. The 36.8% prevalence rate of rifampicin resistant TB and HIV co-infection found in this work is lower than 51.2% reported in Nasarawa [9] but different from studies conducted in Calabar [17], Kwara [8] and Jos [27] who observed comparatively lower co-infection rate.

## 5. STRENGTHS

GeneXpert has highly enhanced the detection of TB cases and is significantly faster and more sensitive than the existing diagnostic methods especially among people living with HIV and MDR-TB.

## 6. LIMITATIONS

This study was hospital-based and patient selection referral bias could not be ruled out. Xpert RIF/MTB Ultra, an improved version of the assay used in this study, is recommended for subsequent studies on MTB detection.

## 7. CONCLUSION

This study showed the presence of rifampicin resistance in the country. Moreover, it showed that the most productive age group in Nigeria economically and socially are seriously threatened and spells unpleasantness for the future of the nation if immediate interventions are not mediated. A high rate of co-infection with HIV was also shown by this study. These are crucial issues that call for immediate serious preventive measures, quick accessibility of diagnosis, treatment and monitoring from the policymakers to avert the impending danger.

## CONSENT

Informed and written consent, suitable sputum sample in the appropriate sample container was provided by each participant. Patients were sufficiently instructed on how to produce the required sample.

## ETHICAL APPROVAL

Ethical permission was sought from the Oyo State Research Ethics Review Committee.

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## COMPETING INTERESTS

Author has declared that no competing interests exist.

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