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Occurrence rate of rifampicin-resistant *Mycobacterium tuberculosis* in patients attending chest clinics in selected hospitals in Akure metropolis

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ABSTRACT

Background: The increase in incidence of *Mycobacterium tuberculosis* (MTB) and emergence of drug resistant strains of MTB is a serious issue especially in developing communities. The aim of this study is to investigate occurrence rate of rifampicin-resistant *Mycobacterium tuberculosis* in patients attending chest clinics in selected hospitals in Akure metropolis Ondo State, Nigeria. **Methods:** A total of five hundred (500) sputum samples were collected from patients attending selected chest clinics in Akure metropolis and a specially designed questionnaire was used to collect the socio-demographic data of the individuals recruited for the study. The collected sputum samples were analyzed using GeneXpert machine (Cepheid, Model GX-IV) to detect MTB rifampicin resistance. **Results:** 51(10.2 %) of the 500 patients screened were positive for MTB while 8(15.7 %) of the MTB positive patients had rifampicin-resistant MTB. The occurrence of rifampicin-resistant MTB was higher in males (23.8 %) than in females (10.0 %). It was also higher among the age range of 20-31 years with percentage of (33.3 %) and higher among singles (87.5 %) than the married (2.3 %). Rifampicin-resistant MTB was higher among the illiterate (20 %). **Conclusion:** It is imperative that the health policy makers and government should increase the awareness campaign on tuberculosis prevention and also encourage more studies for the development of novel and more effective tuberculosis' drugs by financing the project.

Introduction

Mycobacterium tuberculosis (MTB) is the aetiological cause of tuberculosis (TB), an infectious, chronic and debilitating disease. Although this bacterium typically affects the lungs causing pulmonary TB it can also affect other sites as well as causing extra-pulmonary tuberculosis [1]. The disease can spread via aerosol when people with pulmonary TB expel bacteria through coughing [2]. However, a relatively small proportion of people infected with MTB develop tuberculosis disease world health organization (WHO), [3]. The reason

for this is the immune response inherent in the host's system. However, in the presence of immunocompromising diseases like human immunodeficiency virus (HIV), the likelihood of developing the disease increases considerably [4]. Although, tuberculosis can be treated with antibiotics like rifampicin, isoniazid and streptomycin, the emergence of MTB resistance to anti-TB drugs has been a major public health obstacle to achieve a better effective global tuberculosis control [5].

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Drug-resistant MTB arises from spontaneous mutations and can also be enhanced by poor adherence of patients to anti-TB drugs as revealed by **Onyedum et al.** [6]. In 2015, it was estimated that 580,000 tuberculosis cases were resistant to at least rifampicin (RR-TB) and 480,000 of the population were resistant to both rifampicin and isoniazid with 250,000 death occurred [7]. The standard methods for diagnosing tuberculosis are direct microscopy and culturing but are time consuming and have a low sensitivity [6]. Molecular methods however such as the use of GeneXpert is a newer and more rapid method of diagnosis of rifampicin resistance (RR) as reported by **Prasad et al.** [8]. This Genexpert MTB/RIF was endorsed by WHO, [9]. It is a rapid and automated molecular system that detects both MTB DNA and rifampicin resistance simultaneously.

Nigeria has the second highest tuberculosis burden disease in Africa, and according to WHO, [10] Lagos, Kano, Oyo and Benue States have the highest prevalence rates. The study aimed to diagnose tuberculosis in patients attending selected chest clinics in Akure metropolis, diagnose rifampicin-resistance, and the associated risk factors.

Materials and Methods

Study area

Akure is a popular metropolis in Ondo State. The relative humidity averaged 80 % with temperature range between 23 °C and 30 °C Civil servants are the major inhabitants of the city which is the centre of administration of the Ondo State Government. However, farming and trading are other occupation of the residents who majored in food crops and livestock production as stated by **Folayan**, [11].

Study subjects

The study subjects include presumptive cases of tuberculosis who had been coughing for a period of two weeks and above with or without blood-tinged sputum, night sweat, weight loss, fatigue but visiting the clinic for the first time. Both male and female patients of all ages were enrolled for this study. They were administered questionnaires to generate socio-demographic data.

Collection and handling of samples

Five hundred (500) sputum samples from suspected patients with complains of cough that lasted for up to two weeks and above that were visiting selected hospitals; University of Medical Sciences Teaching Hospital (UNIMEDTH), Health Centre Ijoka,

Health Centre Arakale and Nigeria Police Clinic) in Akure metropolis were collected into clean (sterile) wide-mouth universal containers, after health talk on how to collect the sample. The patients then moved to a designated site where there is an open air flow to cough and produce the thick phlegm from the bronchi into the container and cover it with a lid. The samples were then transported into the laboratory for documentation as patient's name; age and serial number were written on the specimen container. Sputum sample were kept inside refrigerator at 4 °C and processed within 24 h.

Detection of rifampicin-resistance *Mycobacterium tuberculosis*

The collected sputum samples were analyzed for the presence of DNA sequences specific for MTB and rifampicin resistance using the GeneXpert MTB/RIF (New Jersey, US) (cartridge-based Nucleic acid amplification test) according to the manufacturer's instruction. Two millilitres (2 ml) of sputum sample was mixed with 2 ml of buffer containing NaOH and isopropanol to liquefy the sputum and incubate at 30± 2 °C for 15 min. Thereafter, 2 ml of the diluted sample was transferred to the cartridge for ultrasonic lysis of mycobacteria to release target DNA. The cartridge was loaded into the GeneXpert machine (Cepheid) to proceed with the rest protocol. After 2h, the comprehensive test result was read on computer screen. Results were automatically generated indicating the presence of MTB or not and whether the bacterium is rifampicin resistant or not (RIF).

Data analysis

Data were analyzed using the Statistical Package for the Social Sciences (SPSS) for window version 16. Chi square test was used to determine the relationship between variables. Obtained figures were statistically significant at $p < 0.05$.

Results

The overall prevalence of tuberculosis in the study area was 10.2 % with 51 out of the 500 samples tested positive for MTB (**Figure 1**).

Out of the 51 sputum samples that are positive for MTB, 8(15.7 %) were resistant to rifampicin while 43(84.3 %) were susceptible to rifampicin (**Figure 2**).

Based on age group, it was observed that high prevalence 2(33.3 %) of rifampicin resistance among patients aged 31 to 40 years and 41 to 50 years (18.2 % for both groups) (**Figure 3**).

Rifampicin resistance was higher in males with prevalence of 23.8 % compared to their females with prevalence of 10.0 % (Figure 4).

Higher frequency of rifampicin-resistant MTB was found among the singles with a prevalence of 87.5% while 2.3% was observed among the married (Figure 5).

Occurrence of rifampicin resistant MTB based on level of education of patients positive for tuberculosis

The illiterates had the highest occurrence (20.0%) for rifampicin resistant MTB while the least (11.8%) was seen in those with only secondary school certificate as there was no occurrence rate observed for higher national diploma (HND) students (Figure 6).

Figure 1. Frequency of occurrence of *Mycobacterium tuberculosis* in the sputum of patients recruited for the study in Akure metropolis.

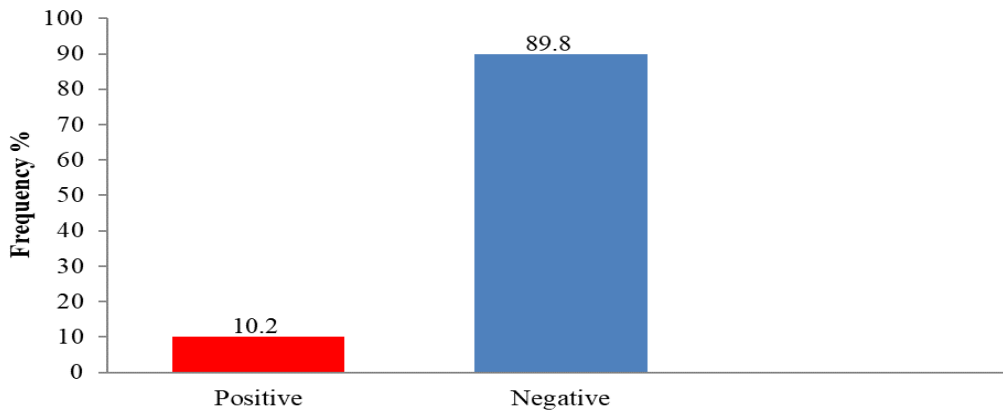


Figure 2. Frequency of rifampicin resistant MTB among Mycobacterium tuberculosis sputum positive samples (n=51).

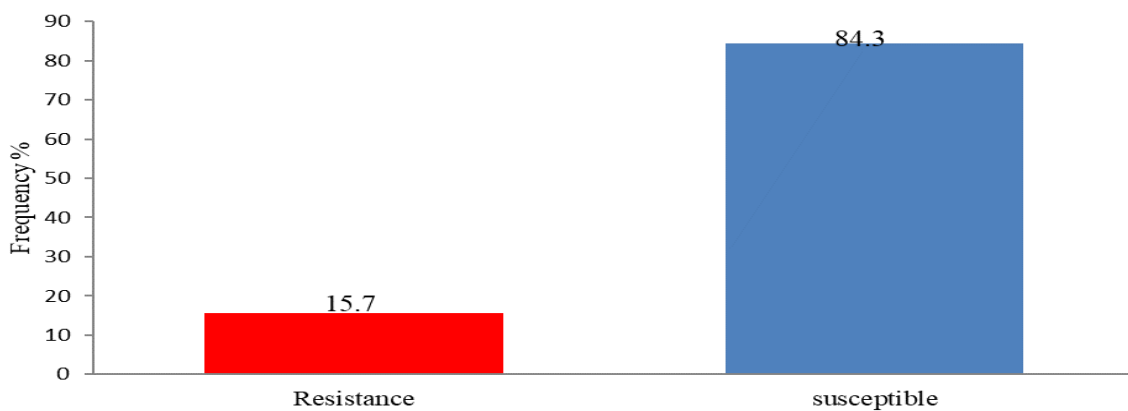


Figure 3. Frequency of rifampicin resistant MTB among different age groups.

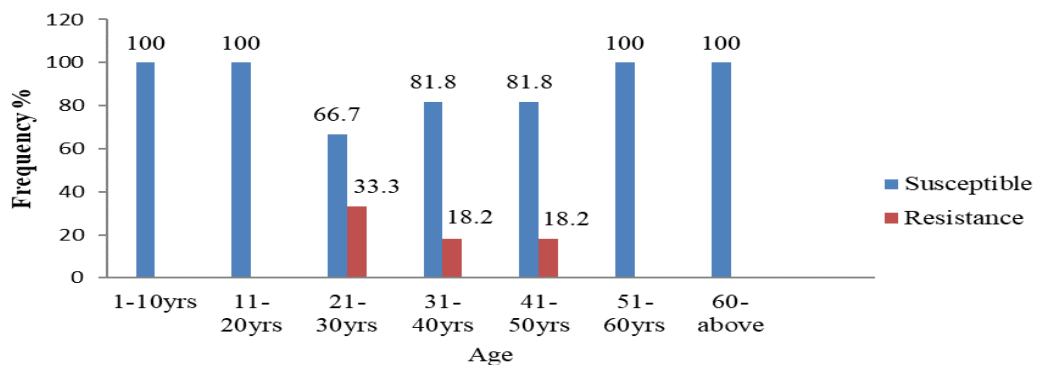


Figure 4. Frequency of rifampicin resistant MTB in male and female patients.

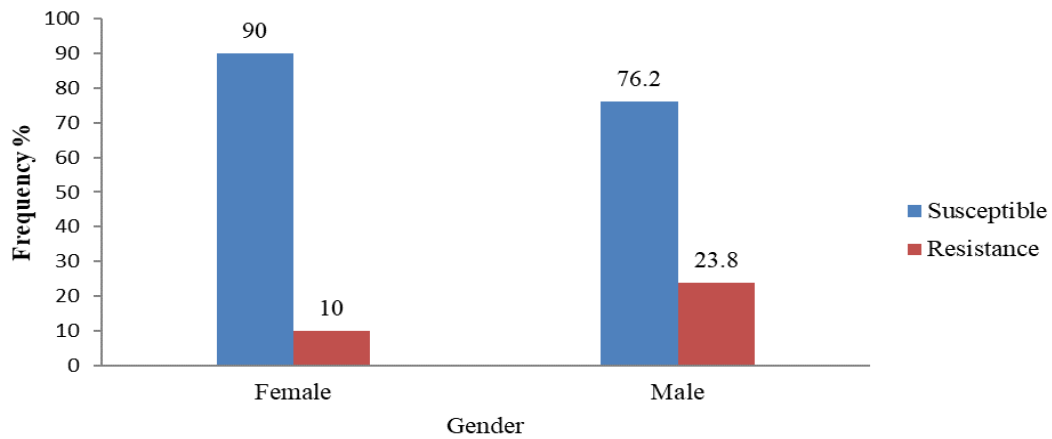


Figure 5. Frequency of rifampicin resistant MTB in single and married patients.

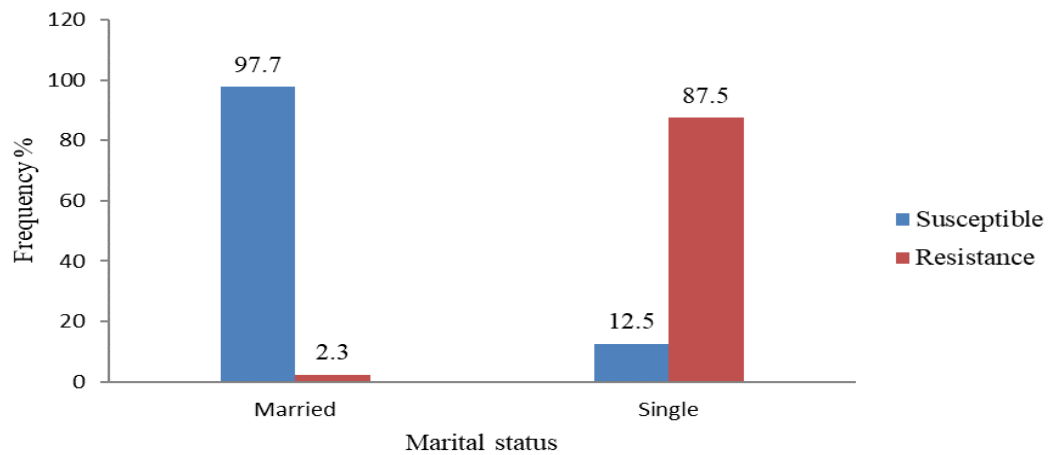
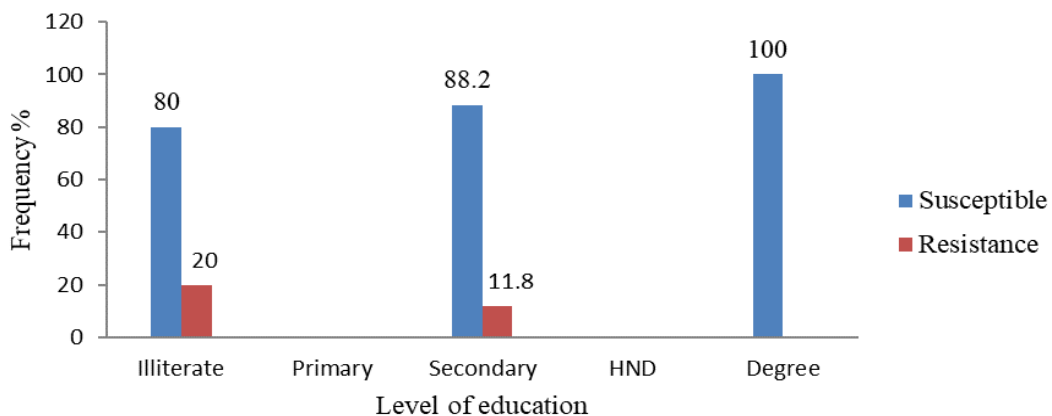


Figure 6. Frequency of rifampicin resistant MTB among different education levels.



Discussion

The occurrence rate of rifampicin-resistant MTB (15.7 %) found in this study was lower than the findings of **Bello et al.** [12] which was 18.8 % in the same community but the study was conducted in only one chest clinic of State Specialist Hospital, Akure. However, the value obtained in this study

was higher than that observed by **Adetunji et al.** [13] who detected rifampicin resistance to be 12 % among HIV patients in Oyo State, Nigeria. Our finding is also higher than that observed by **Okonkwo et al.** [14] who reported low occurrence of 6.9 % in Nnewi, Nigeria. High prevalence rates could be attributed to poor tuberculosis control

practices and non-compliance with preventive guidelines leading to inadequate treatment. Inadequate treatment then leads to a selective pressure that favours the multiplication of mutant organisms, emerging as resistant clones. These clones may continue to replicate in the presence of the sub-lethal dose to become predominant leading to the recrudescence of the disease that is then resistant to the anti-tuberculosis medication [15].

In this study, the highest MTB rifampicin resistance was observed among age group 21-30 years. Similar finding was detected by **Esther et al.** [16]. Based on gender, rifampicin-resistance was higher in males compared to their female counterparts. This agrees with the research work of **Stephen**, [17] who reported that rifampicin-resistance was higher in males than females in Ibadan. The high association of rifampicin resistance in the male gender can be explained by the social life of males such as smoking, alcoholism and related vitamins deficiency. Also poor health-seeking behavior of males compared to females could make them more susceptible as supported by **Danlami et al.** [18]. It was observed from this study that higher frequency of rifampicin-resistant MTB was found among the singles with a prevalence rate of 87.5% while 2.3% was observed among the married.

According to research work done by **Lienhardt et al.** [19], who reported that marital status has long been associated with the risk of developing rifampicin-resistant tuberculosis in Africa and all over the world. Similar findings to this investigation were reported in a study conducted in Guinea-Bissau which illustrated that being single and living alone was independent risk factor for contracting rifampicin-resistant tuberculosis. The high frequency of 20 % MTB resistance observed in illiterates could be due to poor health and living conditions emanating from their ignorance not to indulge in predisposed risk factors of tuberculosis as supported by **Stephen**, [17].

Conclusion

The high occurrence of rifampicin-resistant MTB in Akure, Ondo State, Nigeria therefore underscores the need to improve the treatment of drug resistant MTB cases and thereby reduce the incidence of MTB drastically globally.

Recommendations

There is the need to strengthen the tuberculosis programme by increasing the

awareness of the disease among the populace. Public awareness will enhance early detection of cases in the community for quick commencement of therapy. Development of new drugs that are more effective against MTB is also recommended in order to prevent the emergence of drug resistant tuberculosis.

Ethical consideration

This study was approved by Ondo State Ministry of Health, Akure (OSHREC/18/01/2019/088). Informed consent was also obtained from the patients.

Conflicts of interests: None.

Funding: None.

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