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Research Article

Rifampicin-monoresistant Mycobacterium tuberculosis among the patients visiting chest clinic, state specialist hospital, Akure, Nigeria

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ABSTRACT

Background: Tuberculosis (TB), one of the most important contagious diseases, is a leading cause of death due to a single pathogen worldwide. Co-infection of people living with HIV with M. tuberculosis has been shown to increase the mortality rate in sub-Saharan Africa.
Methods: This present study was carried out to establish the rifampicin resistant profiles among the patients attending chest clinic, state specialist hospital, Akure. We enrolled clinical samples submitted between January 2013 and December 2013 for this study. The sputum samples were analyzed using GeneXpert.
Results: Of the 135 sputum processed by GeneXpert, 48 (35.6%) contained Mycobacteria tuberculosis (MTB) and 9 (18.8%) were rifampicin resistant Mycobacteria tuberculosis. Patients within the age group of 24-32 years showed the highest resistant to RIF 6 (12.5%).
Conclusion: This study has helped to establish that there is presence of rifampicin resistant Mycobacterium tuberculosis in Akure, Ondo state, Nigeria and most of them were observed among patients who default treatment. This is considered as a threat to TB control programme in Akure, Nigeria and it is recommended that strategies should be put in place in order to ensure patients' compliance and monitoring of patients' response to TB treatment.

Keywords: Rifampicin resistant, Mycobacterium tuberculosis, GeneXpert, Akure

INTRODUCTION

Tuberculosis (TB) is one of the most important contagious diseases and a leading cause of death due to a single pathogen worldwide. The tubercle bacilli in patients with pulmonary TB could be spread in droplet aerosols as they cough, sneeze, or even talk and infect those in contact. On the average, a person with untreated pulmonary TB is estimated to infect 10-15 persons annually.[1]

Epidemiologically, African countries have not been faring well in the rate of spread of the infection since late 1980s and this has coincided with the HIV pandemic. Co-infection of people living with HIV with M. tuberculosis has been shown to increase the mortality rate in sub-

Saharan African countries like South Africa, Botswana, and Zambia.[2] Nigeria was ranked fifth as high burden country with tuberculosis according to WHO report of 2008.[3] It is estimated that one-third of the world's population is infected with M. tuberculosis complex,[4] with around 9 to 10 million new cases reported annually.[3]

Rifampicin is one of the most important anti-tuberculosis (anti-TB) antibiotics; it exerts its bactericidal activity by inhibiting the early steps of gene transcription by binding to the ß -subunit of RNA polymerase (rpo ß) encoded by the rpo ß gene.[5] Rifampicin has proven to be an effective anti-tuberculosis agent and its use has greatly shortened the duration of chemotherapy for treatment of TB. In recent years, the control of TB has been impeded by the emergence of drug-resistant M. tuberculosis strains.[6] The problem of TB has been compounded by the emergence of multi-drug resistance M. tuberculosis and Human Immunodeficiency Virus (HIV).

Shortly after the first anti-tuberculosis (TB) drugs were introduced, streptomycin (STR), para-aminosalicylic acid (PAS), isoniazid (INH) resistance to these drugs was observed in clinical isolates of Mycobacterium tuberculosis.[7] This led to the need to measure resistance accurately and easily. The Pasteur Institute introduced the critical proportion method in 1961 for drug susceptibility testing in TB and this method became the standard method of use.[8]

Studies on drug resistance in various countries in the 1960s showed that developing countries had a much higher incidence of drug resistance than developed countries.[8] By the end of the 1960s rifampicin (RIF) was introduced and with the use of combination therapy, there was a decline in drug resistant and drug susceptible TB in developed countries. This led to a decline in funding and interest in TB control programs. As a result, no concrete monitoring of drug resistance was carried out for the following 20 years.[8] The arrival of HIV/AIDS in the 1980s resulted in an increase in transmission of TB associated with outbreaks of multidrug- resistant TB that is, resistant to INH and RIF.[9,10] In the early 1990s drug resistance surveillance was resumed in developed countries, but the true incidence remained unclear in the developing world.[11]

The development of resistance to rifampin is due to mutations in a well-defined, 81 base pair (bp) (27 codons) central region of the gene that encodes the Î²-subunit of RNA polymerase (rpo ß).[12] More than 96% of the rifampin-resistant strains contain a mutation in this 81 bp region of rpo ß, thus facilitating a straightforward approach to detecting rifampin resistance and/or MDR rapidly.[12]

Rifampicin resistant heralds higher rates of treatment failure and death for the patient and a poor outcome if the isolate is also resistant to izoniazid.[6] Efficacy of rifampicin chemotherapy can be markedly reduced when infections are caused by M. tuberculosis strains that are rifampin resistant.[13]

There are scientific publications in different parts of Nigeria on drug resistant Mycobacterium tuberculosis, but none have been reported in Akure, Ondo state.[14,15]

Therefore, this present study was carried out to establish the rifampicin resistant profiles among the patients attending chest clinic, state specialist hospital, Akure.

METHODS

Clinical specimens

Clinical samples submitted between January 2013 and December 2013 were enrolled in this study. One hundred and thirty five (135) patients within the age of 15 and 65 years suspected of pulmonary tuberculosis were included in this study. All clinical samples were drawn from those submitted to the TB laboratory of the chest clinic, state specialist hospital, Akure for pulmonary tuberculosis diagnosis and monitoring. All the samples were sputum.

The patients were categorized as thus; (i) patients that had previously received treatment in the same or another clinic but default after some time (ii) patients whose treatment history could not be assessed, (iii) patients that visit the clinic for the first time and (iv) patients who had relapse after completion of normal treatment plan. A detailed clinical history, sex, and age were collected from the requisition forms that accompanied the samples.

Processing of samples for GeneXpert

The GenXpert MTB/RIF is an automated molecular test which detects DNA sequences specific for MTB and RIF resistance by polymerase chain reaction with fully integrated sample processing in patients suspected of drug sensitive or multidrug resistant pulmonary tuberculosis.

1 ml of sputum sample was mixed with 2 ml of buffer (Cepheid AB Rontgenvagen 5 SE-171 54, Solna) to liquefy the sputum and incubated at room temperature for 10 minutes. Thereafter, 2 ml of the diluted sample was transferred to the cartridge (Cepheid AB Rontgenvagen 5 SE-171 54, Solna) 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 2 hours, the comprehensive test result was read on computer screen.

Statistical analysis

Frequencies, means and the percentages were generated using the Statistical Package for the Social Sciences version 18.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

Of the 135 sputum processed by GeneXpert, 48 (35.6%) contained Mycobacteria tuberculosis (MTB) and 9 (18.8%) were Rifampicin resistant Mycobacteria tuberculosis. Patients within the age group of 24-32 years showed the highest resistant to RIF 6 (12.5%) (Table 1).

Table 1: Age distribution of patients with MTB and RIF resistant in chest clinic, Akure.

Age range (Year)	Frequency (n)	No. positive for MTB (%)	No. of patients with RIF resistant (%)
15-23	18	15	0 (0.0)
24-32	33	15	6 (12.5)
33-41	48	15	3 (6.3)
>41	36	03	0 (0.0)
Total	135	48 (35.6%)	9 (18.8%)

Of the 9 (18.8%) patients with RIF resistant, 4 (8.3%) defaulted treatment and were re-treated, 3 (6.3%) relapsed after completion of normal treatment plan (Table 2).

Table 2: Showing different categories of patients with RIF resistant.

Category of patients	No. of patients resistant to rifampicin
Default patients	4 (8.3%)
Patients with history	1 (2.1%)
First time patients	1 (2.1%)
Relapse patients	3 (6.3%)
Total	9 (18.8%)

DISCUSSION

In vitro resistance to anti-TB drugs was first reported in Nigeria over three decades ago and local health practitioners have the perception that drug resistance has increased in the recent years.[16] This might be due to decline in funding and interest in TB control programs.

In 2010, Rifampicin Mono-Resistant (RMR) tuberculosis accounted for 0.3%, 0.3%, and 0.1% of primary TB cases, and 1.9%, 0%, and 0.2% of secondary TB cases in Germany, United Kingdom, and Poland, respectively.[17]

The prevalence of RIF mono-resistant in this study was 18.8%. This result corresponds with the finding in Abuja, North central part of Nigeria were 19.0% of rifampicin mono-resistant was recorded.[18] Other studies conducted in different parts of Nigeria reported a RIF resistant of 11.8 to 22% therefore; our finding is in tandem with other findings in Nigeria.[14,19,20] RIF resistant reported from America, Western Pacific region and Europe were 2.1%, 4.9% and 12% respectively.[21]

In this present study, rifampicin resistance of 2.1% was observed among first time (new) patients and 8.3% was observed among patients who were re-treated after defaulting treatment. This finding corresponds with 2.2% reported by WHO among the notified newly diagnosed pulmonary TB cases though the report by WHO is higher 9.4% among re-treatment cases.[21,22]

Rifampicin resistance of 2.1% reported among first time (new) patients in this study is low when compared to the 5.52% reported in Jos and Lagos from a study on genetic determinants of drug-resistant tuberculosis among HIV-infected patients.[19] The reason for this difference may be due to the restriction of the study to only HIV/AIDS patients while our study was not restricted to only HIV/AIDS patients.

The data presented in this study showed that the age group with high risk for RIF resistance was 24-32 years. A similar finding was recorded in other regions of the country.[19,20,23]

CONCLUSION

This study has helped to establish that there is presence of Rifampicin resistant Mycobacterium tuberculosis in Akure, Ondo state, Nigeria and most of them were observed among patients who default treatment. This is considered as a threat to TB control programme in Akure, Nigeria and it is recommended that strategies should be put in place in order to ensure patients' compliance and monitor their response to TB treatment.

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