# ARTICLE IN PRESS

# Characteristics of Mycobacterium Tuberculosis Positive Patients Screened for Drug-Resistant Tuberculosis at a Tertiary Health Facility in Lagos, Nigeria

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#### Funding: None.

Acknowledgements: Authors acknowledge the staff of the nursing and medical records departments of LASUTH for their help in retrieving the data used for this study.

Abstract: Background: Nigeria is one of the ten countries with the highest tuberculosis (TB) burden globally and is experiencing an increasing incidence of drug resistance. This study aimed to determine the prevalence of mycobacterium tuberculosis and rifampicin resistance (DR-TB) among patients screened at the TB clinic of a tertiary institution in Lagos, South-West, Nigeria.

Methods: A review of records of 840 patients with suspected drug-resistant TB was carried out from Gene Xpert test clinic register at a tertiary health facility from November 2013 to April 2015. The Data was analyzed with SPSS version 20, Chi square test was used to determine association between DR-TB and the factors examined and the level of significance was set at P < 0.05.

Results: MTB detection among all screened suspects was 43.3%. The prevalence of ifampicin resistance was 17.6% among patients that were investigated for DR-TB and this occurred more in the working age group (15-54 years) with male to female ratio of 1.8:1. However, only history of close contact with known DR-TB patient was associated with DR-TB (P < 0.01).

Conclusion: The burden of DR-TB may be higher than previously thought. Drug resistance testing should be made more available to detect cases and thus control the emerging problem.

Keywords: Drug-resistant TB∎Gene Xpert∎Hospital∎Lagos

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# INTRODUCTION

igeria has one of the highest burdens of tuberculosis worldwide.<sup>1</sup> Tackling this burden has been further complicated with the emergence of multi drug resistant tuberculosis. This occurs when there is a development of resistance to isoniazid and/or rifampicin, the two most effective first-line drugs for tuberculosis. Drug resistant tuberculosis (DR-TB) is more difficult to treat and has longer treatment duration. It is also more expensive to manage since it requires the use of second line drugs and closer patient monitoring. Patient outcomes are also less favorable.<sup>2,3</sup> There is also a possibility of spread to close contacts who may then develop DR-TB as primary infection. Implicated in the development of DR-TB are poor quality drugs, interruption of drug supply and poor patient adherence to drugs as they lead to poor treatment outcomes and increased prevalence of DR-TB in the community.

The World Health Organization (WHO) reports that over three percent of all new TB cases are MDR-TB and it is estimated that MDR-TB was responsible for over 190,000 deaths in 2014. In the same year, Africa had over 25,000 laboratory confirmed cases of MDR-TB with a prevalence of approximately 7%.<sup>2</sup>

In Nigeria, the prevalence reported in different studies varies by location; in Kwara State, northern Nigeria, a prevalence of 7% using hospital-based data was reported,<sup>4</sup> while another study done in South-west Nigeria reported a prevalence of overall resistance to rifampicin only of 46% in new and previously treated TB patients. Furthermore, the authors reported an association between previous anti-TB treatment and MDR-TB but age and gender were not associated with MDR-TB.<sup>5</sup>

In recent years, the development of improved diagnostics and the availability of such equipment in resource limited settings such as Nigeria have made diagnosis of drug resistant TB easier using the Gene Xpert test. The Xpert MTB/RIF is a PCR-based rapid diagnostic test which detects presence of TB bacilli and also rifampicin resistance. The test has been reported to have a sensitivity of 97.6% and specificity of 99.8%.<sup>6</sup>

According to the Nigerian TB treatment guidelines, patients returning after default, treatment failure and HIV co-infected patients are routinely tested for MDR-TB.<sup>7</sup> Extensive research has been carried out on drug-sensitive

#### CHARACTERISTICS OF MTB PATIENTS

TB but there is limited data on the burden of DR-TB in Nigeria. The routine testing for resistance among selected patients presents an opportunity to add to the body of knowledge on the topic. This study had the aim of determining the prevalence of MTB and DR-TB among patients screened at a TB clinic and also to identify the predictors of DR-TB in Lagos State, South-West, Nigeria.

# METHODS

#### Study design and setting

A descriptive study involving the use of secondary data was carried out by analyzing routine data collected at the TB clinic of the Lagos State University Teaching Hospital (LASUTH). The clinic attends to both walk-in and referred patients, serving as a referral center for other TB centers within its catchment area of Ikeja local government area of Lagos State. The services provided in the clinic include management of drug sensitive tuberculosis, HIV counseling and testing, sputum smear microscopy and Xpert MTB/RIF testing.

# Data collection

All patients that were investigated for DR-TB from commencement of Gene Xpert testing in November 2013 till April 2015 were included in this study. The data set consisted of socio-demographic details such as age and gender of patients, test results such as sputum AFB, HIV and MTB/RIF, as well as indications for gene Xpert MTB/ RIF test. The data was extracted using a proforma designed for the purpose without any identifiers.

### Data analysis

The data was analyzed using SPSS version 20 for windows. The results were presented in proportions, Chi square test was used to test the association between variables (age, gender, HIV co-infection and history of contact with person with DR-TB). The level of significance was set at P < 0.05.

The main outcome variable was DR-TB which was based on clients having a positive gene Xpert MTB/RIF, that is, those in whom Rifampicin resistance was detected in their sputum samples.

#### Ethical consideration

The study made use of existing, routinely collected health facility data. Permission was taken for the use of the data from the hospital authorities. Data did not have any identifiers.

# **RESULTS AND DISCUSSION**

A total of 840 patients were screened simultaneously for MTB and DR-TB with the Gene Xpert MTB/RIF during the 18-months period under review. Of this number, 364 (43%) had bacteriologically confirmed TB and thus had reports for drug susceptibility.

The male: female ratio of the patients was 1.8:1. The median age was  $35 \pm 13.4$  years. Less than a third of the patients were within the 25-34 years age group (32.1%). Only 1.9% of patients were children below 15 years and 3.8% were elderly ( $\geq 65$  years). Approximately 12% of the patients gave a history of contact with a confirmed MDR-TB patient. About one in five of the patients (21.2%) were HIV positive. Rifampicin resistance was 17.6% among patients who were MTB positive (Table 1).

Rifampicin resistance was higher among patients who were contacts of known DR-TB patients (35.9%) than patients who gave no history of contact with known DR-TB patients (21.7%) and this difference was statistically significant (P < 0.01, Table 2). This was confirmed using binary logistic regression (Table 3). Age, sex and HIV status were not associated with DR-TB.

Following the endorsement of the MTB/RIF assay by the WHO in 2010, the Nigerian TB control programme commenced the use of the Gene Xpert in diagnosis of

	Frequency (N = 364)	Percentage (%)
Age group		
0-14 years	7	1.9
15-24 years	76	20.9
25-34 years	117	32.1
35-44 years	85	23.4
45-54 years	43	11.8
55-64 years	22	6.0
$\geq$ 65 years	14	3.8
Gender		
Male	234	64.3
Female	130	35.7
MTB (Gene Xpert)		
Detected	364	43.3
Not detected	476	56.7
Rifampicin resistanc	e	
Detected	64	17.6
Not detected	300	82.4

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