ORIGINAL ARTICLE

Rifampicin Resistant Tuberculosis: Prevalence and Risk Factors among Pulmonary Tuberculosis Patients in Maiduguri, Northeastern Nigeria

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ABSTRACT

Background: The introduction of GeneXpert technology for the diagnosis of tuberculosis and detection of rifampicin resistance has revolutionised the efforts of TB control in Africa. Even with this renewed efforts, there is paucity of data on Multidrug Resistant/Rifampicin Resistant Tuberculosis (MDR/RR-TB) in North eastern Nigeria. This study aimed to assess the prevalence of rifampicin resistant-TB and its associated risk factors in this region plagued by insurgency.
Methods: A retrospective review of records of 136 sputum smear positive pulmonary TB cases between September 2014 and January 2017 was undertaken. The sociodemographic and risk factors were obtained from the patients' case notes. Detection of MTB and rifampicin resistance was done using automated polymerase chain reaction (GeneXpert MTB/RIF). Data were analyzed using statistical Package for social sciences (SPSS) version 20; bivariate logistic regression was used to assess associations between various risk factors.
Results: The age range of the patients was 18 to 85 years, with a mean age of 33.1 ±7.67 years. Males constituted a majority (61.8%) of the patients. Overall, 94.1% of the samples from the studied population were susceptible to rifampicin and 5.9% were resistant. Previous use of anti-TB medication was the only statistically significant risk factor associated with rifampicin resistance.
Conclusion: Rifampicin resistant TB is prevalent in our community housing many internally displaced persons, and high index of suspicion is required to avoid its spread. Use of previous anti-TB medication was identified as an independent risk factor for acquisition of rifampicin resistant TB, and this calls for the strengthening of TB control programmes in the region.

KEYWORDS: Tuberculosis, Rifampicin, Resistance, Risk factors Prevalence

Introduction

Tuberculosis (TB) remains a major public health problem worldwide despite advances in diagnostic and therapeutic approaches, with considerable morbidity and mortality. The world health organization reported that about 10.4 million individuals developed TB and 1.8 million died from the disease in 2015[1]. The recent upsurge in TB cases and mortality, has been attributed to co-infection with HIV and rising drug resistance[2]. Other factors found to be associated with TB resurgence in the last decade include lack of implementation of TB control programmes by health authorities and policy makers as well as poverty and increasing population[3]. The upsurge of multidrug resistant (MDR-TB) is posing a threat to the global TB control efforts. Globally, the prevalence of MDR-TB is on the increase in both newly diagnosed and previously treated TB cases[1]. This is a great challenge especially in sub-Saharan Africa, where there is paucity of data on Rifampicin resistant tuberculosis (RR-TB) partly due to

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poor diagnostic tools or poor surveillance and reporting systems. One of the recognized risk factors for developing MDR-TB is previous TB treatment. However, those who have not taken anti-TB drugs in the past are also at increased risk of MDR-TB through acquisition of resistant strains or spontaneous mutations[3].

In its effort to restructure the control of TB in high burden countries like Nigeria, the WHO has introduced GeneXpert MTB/RIF assay, a fully automated nested real time polymerase chain reaction (PCR) system for rapid diagnosis of MTB and detection of rifampicin resistance (as a surrogate marker for MDR-TB)[4,5] In 2015, there was an estimated 480,000 new cases of MDR-TB with additional 100,000 having rifampicin resistance and about 150,000 deaths attributed to MDR-TB. Reports from surveillance data showed that 3.9% of new cases and 21% of previously treated TB cases were found to have RR-TB or MDR-TB in 2015[6].

Nigeria has moved from the 1st to 4th highest TB burden countries in Africa. The incidence of TB in Nigeria is 322 per 100,000 population and in 2015, only 15% of the total TB burden is being notified[1]. With an estimated 3.4 million persons living with HIV in 2014 Nigeria is the second country with the highest HIV burden in sub-Saharan Africa[7]. Reports have shown that about 50-80% of people living with HIV (PLHIV) may be co-infected with TB in Africa[7,8].

The prevalence of MDR/RR-TB in Nigeria is 4.3% among new cases and 25% among retreatment cases[1]. A study from a private care facility in Ibadan reported an MDR/RR-TB prevalence of 53.6%[9], while in Jos Plateau, MDR/RR-TB was found in 4% of new cases and 18% of retreatment cases[10,11]

North eastern Nigeria has the worst health and socioeconomic indices in the country, and the Boko haram insurgency has further worsened this problem. The region is housing about 981,416 internally displaced people (IDPs) because of the insurgency[12]. The IDPslives in camps where spread of infections like PTB are common[13].

Unfortunately, there is scarcity of data on DR-TB in Borno state. This can be due to lack of previous treatment documentation; especially data on patients who have stopped TB treatment, with subsequent relapse or failure due to the aforementioned peculiarities.

The researchers aimed to report on the prevalence of rifampicin resistance among newly diagnosed patients with PTB using GeneXpertwith the likely associated risk factors from ourenvironment.

Materials and Methods

This was a retrospective study of 136 sputum smear positive PTB patients attending the University of Maiduguri Teaching Hospital, Maiduguri, a tertiary hospital located in Northeastern Nigeria between September 2014 and January 2017. All the samples were processed in the microbiology department of the hospital according to standard operating procedure for the GeneXpert MTB/RIF assay. Thereafter the samples were analysed for MTB and rifampicin resistance using the automated GeneXpert MTB/RIF assay machine. Results of the GeneXpert test were automatically generated indicating if MTB was detected or not detected. Where MTB was detected, the GeneXpert automatically generated result indicating if the MTB was rifampicin resistant or not.

The sociodemographic characteristics of the patients (gender, age, residence, religion, occupation, marital status, income, ethnicity and educational status) and possible risk factors were obtained from their case records. Patients' HIV status was obtained from the TB unit register at TB clinic and from the case files of admitted patients.

Data were analyzed using SPSS version 20.0, and results presented in tables as frequencies and percentages. Bivariate logistic regression analysis was used to assess association between the variables (gender, age, residence, religion, occupation, marital status, and education status) and possible risk factors (HIV, smoking). A P-value? <? 0.05 was considered as statistically significant.

Ethical clearance: The University of Maiduguri Teaching Hospital ethical committee approved the conduct of the study.

Results

One hundred and thirty-six sputum-smear positive patients were included in the study. The mean age of the patients was 33.1 (±7.67) years, range 18 years to 85 years. Males constituted 61.8% of the study participants. Majority of the patients were in the age range of 30-39 years, accounting for about 31.5%.Out of the 136 patients, 28(20.6%) were traders and 20(14.7%) were farmers. Over 2/3 of the population (70.6%) were married. Most of the patients (39.7%) had no formal education (Table 1).

Table 1: Sociodemographic characteristics of the study subjects

Variables	Frequency (n=136)	Percentage (%)
Age		
10-19	10	7.3
20-29	36	26.5
30-39	53	39.0
40-49	27	19.9
50-59	3	2.2
60-69	3	2.2
70-79	2	1.5
80-89	2	1.5
Gender		
Male	52	38.2
Female	84	61.8
Education		
Non-formal	54	39.7
Primary	25	18.4
Secondary	31	22.8
Tertiary	26	19.1
Occupation		
Trader	28	20.6
Civil servant	33	24.3
Farmer	20	14.7
Housewife	29	21.3
Student	26	19.1
Marital status		
Divorced	5	3.6
Married	96	70.6
Single	35	25.7

Prevalence of Rifampicin Resistant TB

The overall prevalence of RR-TB in this study was 5.9% (8/136). Majority of those with RR-TB were young males (62.5%, age range of 20-39 years). Majority of the RR-TB weremarried farmers (60%). Out of the 8 patients who had RR-TB, 6 were previously treated for TB and 2 were co-infected with HIV (25%).

Risk factors for RR-TB

The relationship between RR-TB and the various risk factors thought to be important were evaluated using the logistic regression model. Previous history of anti-TB treatment was the only risk factor found to have a significant association with the acquisition of RR-TB (OR: 4.873, 95% CI: 1.975 - 34.512 p=0.023). However, other variables like HIV status, cigarette smoking, occupation and educational level showed no significant association (Table 2).

Table 2: Risk factors associated with the RR-TB among Pulmonary TB cases

Risk Factors	p-value	Crude OR	95% Confidence Interval for OR Lower Bound	Lower Bound
Gender				
Male	0.698	1.358	0.289	6.386
Female		1	1	1
Residence				
Rural	0.113	0.978	0.879	1.435
Urban		1		
Occupation				
Farmers	0.900	0.287	0.193	3.037
C/Servant	0.972	0.280	0.856	2.988
Others	0.911	1		
Education Level				
Non-formal	0.852	2.713	0.321	3.234
Primary	0.827	1.366	0.622	2.253
Secondary	0.875	3.565	0.317	4.872
Tertiary	1	1	1	1
Previous anti-TB treatment				
Yes	0.023	4.873	1.975	34.512
No				
HIV status				
Yes	0.623	1.181	0.597	4.900
No		1		
Smoking				
Yes	0.842	0.797	0.085	7.466
No		1		

Discussion

This study underscores the importance of DR-TB in this part of the country. Early in the 1970s, some studies have reported on the prevalence of resistance to individual anti-tuberculosis drugs like isoniazid and streptomycin in newly diagnosed TB patients in Nigeria[14]. Genetic mutation has been shown to be the reason behind drug resistance for all first line drugs and it is most likely linked to drug misuse[15].

In this study, we demonstrated that the overall prevalence of RR-TB in our patients was 5.9%. This is comparable with previous studies in Nigeria that reported a prevelance of 7.1% and 8.6%[18,14]. A much higher prevalence of 19% in Abuja, Nigeria[10]. However, high sensitivity of the automated culture system used in the later might explain the higher prevalence reported. The number of rifampicin resistant cases was found to be more among males compared to females. This finding is comparable with several other reports from Nigeria and other parts of the world[17-20].Among the various risk factors identified, previous history of TB treatment was found to have a statistically significant association with RR-TB as shown in table 2. This result is in keeping with a previous report from the southwestern part of Nigeria that showed a significant association between previous use of anti-TB medication and drug resistant TB[21]. This relationship may be exolained by the fact that prior exposure to anti-TB drugs will in addition to inhibiting the growth of susceptible bacteria, allow for the selection of preexisting drug resistant mutants to multiply.

Of note is the lack of a significant association between rifampicin resistance and HIV infection in this study. The relationship between HIV infection and MDR/RR-TB has been reported in other studies. Except for reports from studies in Latvia and Ukraine, no association between MDR/RR -TB and HIV co-infection was reported[22]. Similarly, Spellman et al concluded that HIV co-infection was not a risk factor for the development of MDR-TB[23].

Conclusion

The high prevalence of MDR-TB in this study highlights the burden of the condition in our region. There is the need for further studies on drug susceptibility using culture-based techniques to ascertain the actual magnitude, and the driving forces for RR-TB infections in north eastern Nigeria. The study further demonstrated that previous anti-TB medication is an independent risk factor for the development of RR-TB. This calls for an improvement in the existing TB programme towards strengthening adherence by patients accessing the facility for TB treatment.

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