

Prevalence and Factors Associated with Rifampicin Resistant Pulmonary Tuberculosis among Presumptive Patients in Kano State, Nigeria

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Abstract: Rifampicin-resistant tuberculosis (TB) is an emerging problem of great importance to public health worldwide and together with multidrug-resistant TB causes higher mortality rates than drug-sensitive tuberculosis. Data regarding drug-resistance and risk factors associated with rifampicin resistant from Kano are lacking. The study therefore, determined the prevalence and risk factors associated with rifampicin-resistant tuberculosis (RR-TB) in Kano State, Nigeria. A one-year retrospective study was conducted among tuberculosis patients attending Direct Observed Treatment Short-course centers equipped with GeneXpert facilities in Kano State, Nigeria from January 2019 to December, 2019. Pulmonary and extra-pulmonary samples were analyzed using Xpert MTB/RIF assay (Cepheid, GeneXpert, USA). The data was collected from the Xpert MTB/RIF assay registers and patient's folder. Data generated were analyzed using Chi-square and results were presented in tables. Out of 55,021 samples analyzed, 111 (0.2%) had rifampicin-resistant tuberculosis. There was significance relationship between socio-demographic characteristics (gender, age groups and marital status), prevalence and transmission dynamic of rifampicin resistant among the studied subject in the study area (Odds Ratio [OR] = 0.37, 2.54, 1.51; $p \leq 0.5$). The study confirmed the presence of rifampicin resistant tuberculosis in the study area. It also identifies the need to strengthen the laboratory capacity for early diagnosis of RR-TB as well as improvement on availability and accessibility of the services to patients by the relevant authorities to reduce the disease burden.

INTRODUCTION

The emergence of rifampicin-resistant tuberculosis (RR-TB) has been a major obstacle to TB control programme in Nigeria (FMOHN/NTBCP, 2018). A World Health Organization (WHO), report indicated that 580,000 new cases of RR-TB were identified in 2015; and an estimated 250,000 RR-TB patients died in 2015 (WHO, 2018). Although there has been an increase of RR-TB case notifications, gaps remain in case detection and treatment due to under reporting in Nigeria. Nigeria ranked 6th among 22 high TB burden in the world and one of the highest in Africa (Mohammad *et al.*, 2017). A meta-analysis of the prevalence of

rifampicin resistant TB (RR-TB) in Nigeria indicated that 6% of newly diagnosed TB cases had drug-resistant TB (WHO, 2016). GeneXpert® MTB/RIF (Cepheid Inc. New Jersey, USA) for *Mycobacterium tuberculosis* (MTB) and rifampicin resistant TB (RR-TB) detection was endorsed by the WHO in 2010 (Onyedum, *et al.*, 2017; Shao *et al.*, 2011). The Xpert MTB/RIF is a point-of-care real time polymerase chain reaction (PCR) automated diagnostic test that can identify the DNA of *Mycobacterium tuberculosis* (MTB) and rifampicin resistant TB. It has the sensitivity and specificity of 97.6% and 99.8% respectively (Van Rie *et al.*, 2010).

Xpert MTB/RIF assay commenced in Nigeria in 2012 and the programme was implemented by the KNCV Challenge TB with the support of the United States Agency for International Development (USAID) under the supervision of the National Tuberculosis Control Programme (NTBLCP) (Geleta *et al.*, 2015; FMOHN, 2018). The use of Xpert MTB/RIF assay commenced in 2013 in Kano State with few sites, currently the state had 18 Gene Xpert sites. The National tuberculosis control programme made MTB/RIF assay as a baseline entry point for presumptive TB treatment enrollment in Nigeria.

Thus in an effort to identify where TB control efforts should be addressed the study aimed at determined the prevalence and risk factors associated with rifampicin resistant among patients with tuberculosis in Kano State, Nigeria.

MATERIALS AND METHODS

Study area

This study site comprised 18 GeneXpert sites in Kano State, Nigeria. Kano State has forty-four local government areas with a projected population of over 15 million, with more than fifteen thousand confirmed TB cases. The State has one (1) infectious disease hospital, a teaching hospital, an orthopaedic hospital, three referral hospitals and over five thousand private and public health facilities. According to national guidelines, confirmed RR-TB patient will spend 8 months in the intensive phase taking Levofloxacin, Cycloserine, Prothionamide, Kanamycin / Capromycin, Pyrazinamide and Pyridoxine and 12 months in the continuation phase on Kanamycin or Capromycin. HIV counseling and testing were offered to all presumptive TB patients attending DOTS clinics in the State. Patients diagnosed with HIV co-infection will be placed on two (2) weeks anti-retroviral drugs, while children diagnosed with RR-TB will also be placed on the same treatment and time while the tablets will be compounded based on their body weight.

Study design

A one-year retrospective study was conducted; information for the study was obtained by reviewing Presumptive TB registers for Xpert MTB/RIF assay, rifampicin resistant TB; cases and TB patient's folders from January, 2019 to December, 2019.

Ethical issues

Ethical approval for the study was obtained from institutional review board of Aminu Kano Teaching Hospital, Kano, Nigeria (NHREC/28/01/2020/AKTH/EC/2880) and Kano State Ministry of Health Institutional Review Board ethics committee (MOH/Off/797/T.I/2067). Permission for data collection was obtained from medical directors and head of the laboratory services prior to data collection.

Data collection

Data for the study was generated from both soft and hard copies (from the genexpert machines and patients folders) were collected from eighteen (18) genexpert sites and DOTS clinics respectively by the research assistant from each site of Kano State, from January, 2019 to December, 2019.

Data analysis

Data collected were entered in to excel spread sheets, a total of 0.1% with incomplete data were removed. Chi-squared test was used for categorical variables and $P \leq 0.05$ was considered significant. Odds ratio was also calculated to determine the extent of association between the studied risk factors and RR-TB prevalence.

RESULTS

A total of 55,021 presumptive patients were screened using Xpert MTBRIF assay during the 12-month period of the year 2019, out of which 111 (0.20%) had rifampicin resistant. Males had the highest prevalence of 0.15% while females had 0.05% (OR = 0.37; 95% CI, 0.24 – 0.56; P = 0.03) (table 1). Age group ≤ 15 years had RR-TB prevalence of 104 (0.19%) while age group ≥ 15 years had 0.01% (OR = 2.54; 95% CI, 1.18 -5.45; P = 0.02) (Table 1).

There were more rifampicin resistant TB cases among married studied population 60 (0.11) than unmarried 51 (0.09%) (OR = 1.51; 95% CI, 1.02 – 1.03; P = 0.04) as shown in (Table 1). Among the studied TB cases the unemployed had the highest prevalence of rifampicin resistant TB of 91 (0.17%), followed by those employed 20 (0.04%) (OR = 1.26; 95% CI, 0.78 – 2.05; P = 0.40). Non-formal educated TB patients in

this study had the higher RR-TB prevalence of 72 (0.13%) while those with formal education had 39 (0.07%) (OR = 1.11; 95% CI, 0.75 - 1.65; P = 0.65). This study therefore, demonstrated a significant relationship between gender, age group distribution and marital status with rifampicin resistant TB transmission among the studied population ($p \leq 0.05$) (Table 1).

Table 1: Socio-demographic characteristics and risk factors associated with primary drug resistant tuberculosis (n=55,021).

Demographic Factors	No. of Respondents	Prevalence (%)	95% CI Lower Upper	OR	P-value
Gender					
Male	28,139	82 (0.15)	0.24 – 0.56	0.37	*0.03
Female	26,882	29 (0.05)			
Age group					
≤15 years	8,022	7 (0.01)	1.18 – 5.45	2.54	*0.02
>15 years	46,999	104 (0.19)			
Marital status					
Married	35,240	60 (0.11)	1.02 – 1.03	1.51	*0.04
Unmarried	19,781	51 (0.09)			
Employment status					
Employed	11,971	20 (0.04)	0.78 – 2.05	1.26	0.40
Unemployed	43,050	91 (0.17)			
Educational status					
Formal	20,715	39 (0.07)	0.75 – 1.65	1.11	0.65
Non formal	34,306	72 (0.13)			

***Statistically significant**

Table 2 shows that among studied TB cases the prevalence of RR-TB was significantly higher among patients that had contact with other TB cases (5.28%) than those without (0.105%) (OR = 0.02; 95% CI, 0.01 – 0.02; P = 0.00) (Table 2). Also the RR-TB prevalence was significantly higher among patients that smoked (3.529) than the non-smokers (0.138%) (OR = 0.05; 95% CI, 0.02 – 0.05; P = 0.00) (Table 2). Similarly the

prevalence of RR-TB was significantly higher among patients that consume alcohol than those that did not (OR = 0.04; 95% CI, 0.02 – 0.06, P = 0.00), patients with HIV co-infection than those with TB infection alone (OR = 0.12; 95%CI, 0.07 – 0.17; P = 0.00) and those that had diabetes than those without diabetes (OR = 0.04; 95% CI, 0.02 – 0.06; P = 0.00) (Table 2).

Table 2: Factors associated with Rifampicin Resistant TB infection among study population (n=55,021).

Population (n=55,321):					
Factors	Number tested	Prevalence (%)	95% CI Lower Upper		OR P-value
Contact with TB					
Patient					
Yes	1,021	54 (48.6)	0.01 – 0.02		0.02 *0.00
No	54,000	57 (51.4)			
Smoking:					
Yes	1,021	36 (32.4)	0.02 – 0.05		0.04 *0.00
No	54,000	75 (67.6)			
Alcohol					
Yes	639	25 (22.5)	0.02 – 0.06		0.04 *0.00
No	54,382	86 (77.5)			
HIV status					
Positive	2,459	32 (28.8)	0.07 – 0.17		0.12 *0.00
No	52,562	79 (71.2)			
Diabetes					
Yes	1,311	40 (36.0)	0.02 – 0.06		0.04 *0.00
No	53,710	71 (63.9)			

***Statistically significant**

DISCUSSION

This study confirmed the existence of RR-TB among presumptive TB patients attending DOTS clinics in Kano State, Nigeria. Compared with the 4.3% MDR-TB/RR-TB cases estimated for Nigeria by WHO (2017), the findings of this study reported lower RR-TB rate of 0.20% among the studied patients. Although this reported RR-TB prevalence is low among the studied subjects are presumptive TB patients indicating that these category of the patients have already acquired primary drug resistant TB even before being placed on treatment schedule and could become a source of transmitting drug resistant TB bacilli in the community.

Other studies reported a higher RR-TB prevalence of 5.9% in Lagos and its environs (Davies-Bolorunduro *et al.*, 2020). This difference in the prevalence rate in two States could be attributed to the rate of detection of the RR-TB which directly depends on the number of GeneXpert facilities in the two areas. National update reports by NTBLCP, (2018) indicated that Lagos State has 30 geneXpert machines

while Kano has 18 as such this variation in number of facilities could explain the difference in the rate of prevalence between the two States. Additionally, Davies-Bolorunduro *et al.* (2020) explained that the higher RR-TB prevalence reported in their study may be connected to the study setting as the Centre for Tuberculosis Research which serve as the National TB Reference Laboratory were most presumptive DR-TB patients are referred from other hospitals is situated in the area where study was conducted.

The study findings revealed that males had higher RR-TB prevalence than females. This observation is consistent with WHO report that TB affects people of both sexes in all age groups but the highest burden is in men (57%) aged ≥ 15 years (WHO, 2019). The gender difference in the prevalence of RR-TB in the study area could be related to culture and tradition. In an earlier study, poor health seeking behavior among men, social stigma and cultural habits were adduced for the high prevalence of RR-TB among men (Sanders *et al.*, 2006).

In a related study by Aminu and Tukur (2016) revealed that 84.09% of the studied RR-TB patients were males while 15.9% were females. Studies from Southern part of Nigeria and other part of Africa showed that the prevalence of RR-TB was significantly among males (FMOHN, 2011; Adane *et al.*, 2015).

Beside gender, age group and marital status are some of demographic factors that were found to be significantly associated with RR-TB prevalence in the study area. Patient aged greater than >15 years (OR = 2.54; P = 0.02) and those that are married (OR = 1.51; P=1.51; P=0.04) had higher prevalence of RR-TB. The findings of this study are in agreement with WHO's observation that majority of TB cases occur among people aged >15 years (WHO, 2019). Aminu and Habib (2019) opined that this may not be unconnected with fact that patients in this age category are physically active and may be engaged in various sectors of life working experiences as such becoming more exposed to acquire and develop TB.

The findings of this study revealed that some of the risk factors that are found to be significantly associated with RR-TB prevalence include: patients that had contact with other TB cases (OR=0.02; P=0.00) patients that smoked (OR=0.05; P=0.00) and patients that consume alcohol (OR=0.04; P=0.00). In a related study Adesokan (2014) identified contact with TB patients among other factors as significant potential in transmission of TB. In an earlier study Lawal *et al.* (2009) revealed that, overcrowding, poor nutrition. Poor hygiene and ventilation are some of the factors that promote tuberculosis. The observation of this study also agrees with previous studies conducted by Bai *et al.* (2006); Alavi-Naini *et al.* (2012); Ariyothai *et al.* (2004) that cigarette smoking is associated with lung infections, predisposing the smoker to tuberculosis infections of all forms. The findings of this study also agrees with the reports of American addiction centers (2018) and WHO, (2017) reported that alcohol

abuse increase the risk of contracting tuberculosis.

The findings of this study further indicated that, the prevalence of RR-TB is significantly associated with HIV infection (OR=0.12; P=0.00) as patients with HIV co-infection reported higher RR-TB rates. The observations of this study that patients with HIV co-infection had higher RR-TB prevalence rate is not surprising as previous studies in literature have indicated that HIV predisposes to acquisition and development of TB. In a study, Aminu, (2020) explained that the effect of HIV as witnessed among the TB patients reduces body's peripheral lymphocytes especially the CD4⁺ cells which are subset of T lymphocytes that serve as major effector cells that counteract TB infections. Thus the depletion of these cells leads to increase in the acquisition and transmission of TB.

Review literature indicated that diabetes mellitus is one of the important non communicable disease associated with TB. Result of meta-analysis revealed that 15% of TB patients in Nigeria are co-infected with diabetes (Alabel *et al.*, 2019). The observation of the present study also indicated that the prevalence of RR-TB is significantly associated with diabetes as patients with this condition had significantly higher RR-TB prevalence (OR=0.04; P=0.00) compared to TB patients without diabetes. This implies that there is need to screen all TB patients for the presence of diabetes as earlier detection is key to successful management.

CONCLUSION

The study confirmed the presence of rifampicin resistant tuberculosis in the study area; although the reported RR-TB prevalence is low among the studied subjects, yet it poses a potential public health concern. The reported RR-TB prevalence among the studied patients was found to be significantly associated with gender, age, marital status, cigarette smoking, alcohol consumption, HIV infection and diabetes.

The study advocates the need for additional RR-TB detection facilities in the study area for rapid and earlier detection of RR-TB to ensure prompt management of infected TB

cases and this will go a long way in reducing the rate of transmission of drug resistant TB as well as ensuring effective and successful TB control.

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