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Impact of socio-demographic factors on prevalence of rifampicin resistance among patients attending some hospitals in Yobe state of Nigeria

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Abstract

Rifampicin resistance in Mycobacterium tuberculosis is a public health concern in many countries including Nigeria. There is an increase of multidrug resistant tuberculosis which results to morbidity and mortality among presumptive tuberculosis patients. Data regarding Rifampicin resistant tuberculosis in the study area are lacking. A one year prospective, cross-sectional, laboratory based study was carried out among patients attending Direct Observed Treatment Short course in Damaturu, Gashua and potiskum specialist hospitals, Yobe State, Nigeria; from January, 2020 to December, 2020. Sputum samples were collected from consented / assented participants and analyzed using MTB/RIF assay (Cepheid, GeneXpert USA). The data were analyzed using Person Chi-Square and p≤0.05 considered the presence of significant relationship and results were presented in tables and charts. Out of 400 studied participants, males had a prevalence of 2.5% (10/400) while females had 0.8% (3/400). Age group 30-39 years had the highest prevalence of 1.5%. The results show significant relationship between age, gender, and marital status, in the study area. This study confirmed the presence of Rifampicin resistant tuberculosis in the study area. Therefore, there's need to have a public health awareness and strengthen the laboratory capacity for diagnosis and make the services available and accessible to the patients who need them.

Keywords: Age; Gender; HIV status; Pulmonary Tuberculosis; Rifampicin Resistance Tuberculosis; Yobe State; Nigeria

1 Introduction

Pulmonary tuberculosis (PTB) is a chronic infectious air borne disease caused by a group of acid-fast bacteria called Mycobacterium tuberculosis complex (MTC). Despite WHO, 2019 launched "Community informant" approach to identify undiagnosed TB patients in Nigerian communities, 8% of the 4.3million undiagnosed TB patient worldwide are in Nigeria (Ugwu et al., 2021). The fact that Nigeria is one of the ten countries responsible for 77% of the global shortfall in TB case identification and notification in 2016 only serves to worsen the problem (Ugwu et al., 2021). PTB remains a major public health issue, as one third of the world's population has latent TB with 10% of this population developing active disease during their lifetime (Nhamoyebonde, 2014). PTB Ranked as one of the major causes of morbidity and mortality among infectious disease globally (WHO, 2018), prevention of PTB diagnosis and treatment has been complicated by the emergence of drug resistant strains (Mohammad et al. 2017). The threat posed by multidrug-resistant tuberculosis (MDR-TB) to the advancements made in TB control over the years has caused MDR-TB to become significant public health issue worldwide (Bakare et al., 2021)

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The discovery and usage of anti-TB drugs for the treatment of TB diseases brought about enormous relief that is presently being threatened by the emergence of resistant strains of these pathogens (WHO, 2017). Drug resistant MTB can be grouped as Mono (resistant to one anti-TB drug), Multi (resistant to rifampicin and isoniazid) and pre-extensively DR-TB (resistant to any aminoglycoside or fluoroquinolones) and extensive (resistant to fluoroquinolone and any aminoglycosides (second line injectable drugs: amikacin, capreomycin and kanamycin) (Ullah, 2016). Rifampicin is the most important drug in the chemotherapy of tuberculosis (Reddy, 2017). It is one of the two key drugs for short course therapy (0-6 months) and has reduced toxicity. Thus, it encourages patient compliance as well as eliminates the need for long term therapy (18-24 months) (Ikuabe, 2018). Rifampicin mono resistance is rare. It is mostly observed in association with resistance to isoniazid (Jaleta, 2017). Mohammad et al. 2017; reported that, about 90% of rifampicin resistance PTB are multi drug resistant TB (MDR-TB). WHO, 2016 reported that, the global prevalence of DR-TB was 3.8% among presumptive TB Patients and 20% among re-treated TB patients (Kome, 2018). The overall pooled prevalence of MDR-TB among presumptive TB patients in Nigeria was 6.0% (Kome, 2018). Nigeria ranks sixth out of 22 high TB burden and has highest burden of TB in Africa (WHO, 2016; Kome, 2018; Mohammad et al. 2020).

Factors associated with higher risk of MDR-TB apart from TB relapse are exposure to sub optimal anti-TB regimens during previous treatment, due to poor compliance, improper prescriptions and drug storage and quality all these may significantly contribute to the emergence of drug resistant TB (Oneydum, 2017). Also, patients may be treated with irrational fixed dose combinations not adjusted to appropriate body weight, intermittent TB treatment as used in the program has also been associated with a higher risk of acquired rifampicin resistance especially among people living with human immuno-deficiency virus (PLHIV) (Rakesh, 2016). The Xpert MTB/RIF assay is a WHO endorsed point of care molecular assay that is able to assess simultaneously for the diagnosis of MTB and rifampicin resistance within 2hours (WHO, 2011). It is a cartridge based nuleic acid amplification test which is automated and can isolate the genomic material of MTB via sonication, amplify via PCR and identify using fluorescent probes called molecular beacons (Boehme, 2010). Xpert MTB/RIF (cephad), a computerized molecular test for the detection of MTB and RIF resistance directly from clinical specimens is one of the most widely used molecular tests for the diagnosis of TB globally (Huang et al., 2022)

In this test specific sequence of the rpoB gene is amplified with no cross contamination issues (Venter et al., 2017). In 2017 WHO approved XPERT MTB/ultra as the initial TB diagnostic test for adults and children, regardless of HIV status (WHO, 2017). The XPERT MTB/XDRTB PCR-based cartridge introduced in 2020 is another one that has been created for the purpose of detecting mutations linked to XDR-TB or TB that is resistant to several first and second line medicines (Huang et al., 2022). Community based treatment regarding MDR-TB patient has been put into practice with effectiveness in Africa (FMOH, 2017).

Treatment failure associated with PTB has been on increase and this is largely attributed to drug resistance and poor adherence to anti-TB drugs. This study aims to measure the prevalence of rifampicin resistant tuberculosis among presumptive TB cases of in Yobe State Nigeria, to determine the correlation between rifampicin resistant TB acquisition and spatial distribution of the disease in the study area.

2 Material and methods

2.1 Study Area and Population

The study was conducted in Yobe state in North East, Nigeria. Yobe state was curved out from the Borno state in 1991. The state is an agricultural producing state with diverse solid minerals resources. It has a projected population of four million five hundred thousand two hundred and fifty (4,500,250) (NPC 2006) the state is multi ethnic and Damaturu is the State capital, with a land mass of 45,502 km2; it is bounded by Borno, Bauchi and Jigawa States.

2.2 Study Designed

This is a cross-sectional, prospective and laboratory-based study.

2.3 Sampling Frame

The directly observed treatment short course (DOTS) centre for each of the three senatorial zones of the state was purposively selected to ensure adequate sampling and appropriate representation. These centers were State Specialist Hospital Damaturu (Yobe zone A), General Hospital Potiskum (Zone B) and General Hospital Gashua (Zone C). Patients with suspected cases of PTB were seen at the DOTS center of the selected facilities and educated on how to produce sputum sample for analysis. A sterile, wide mouth and transparent container was used for sample collection.

The samples were sent immediately to the Gene Xpert laboratory for analysis in a cold box containing ice pack;

2.4 Inclusion and Exclusion Criteria

Only those participants that were consented or assented to participate in the study from January 2020 through December, 2020 were included. While patients attending other clinics and those that did not agreed to participate in the study were excluded.

2.5 Data Collection and Management

Socio-demographic characteristics, some factors associated with tuberculosis infection and spatial distribution of the disease in the study area were collected using structured questionnaire. Data recorded were analyzed using Chi-Square, and descriptive statistic and P value lesser than or equal to 0.05 ($p \leq 0.05$) was regarded as significant statistically.

A total of 400 participants were recruited during the stud

2.6 Ethical Clearance

Ethical approval to carry out this study was obtained from institutional review board ethics committee (MOH/GEN/747/VOL.1).Permission to carry out this study was obtained from Medical Directors and HOD of the laboratory and DOTS centers in-charge prior to samples collection and analysis

3 Results

A total of 400 studied participants comprising of 255 (63.8%) males and 145 (36.2%) females; 79 (19.7%) were eligible for the study. 79 (19.7%) were found with pulmonary tuberculosis, out of which 13(3.3%) had rifampicin resistant tuberculosis. Age grade 20-29 years participants accounted for much of the study population 96 (24%). HIV positive individuals were 20 (0.5%) while those residing at Gashua, Yobe Zone C, get the highest zone-based number of participants. Table 1 summarizes the characteristics of studied population.

Table 1 Characteristics of Studied Participants

Variables	Frequency	Percentage (%)
Age Group(Years)		
10-19	32	1 (0.3)
20-29	96	3 (0.8)
30-39	93	6 (1.5)
40-49	75	2 (0.5)
50-59	56	1 (0.3)
≥60	48	0 (0.0)
Gender		
Male	255	10 (2.5)
Female	145	3 (0.8)
HIV Status		
Positive	20	2 (0.5)
Negative	358	11 (2.8)
Unknown	22	0 (0.0)
Location of Residence		
Damaturu	127	5 (1.3)
Potiskum	114	6 (1.5)
Gashua	159	2 (0.5)

A prevalence of 3.3% (13/400) was recorded for rifampicin resistant PTB details are shown in the table 2.

Prevalence of rifampicin resistance in relation to other study variables (age, gender, retroviral status and location of residence) gave different figures as shown in table 3. Age grade 30-39 years gave the highest age-based prevalence 1.5% which was closely followed by 0.8% recorded for age-grade 20-29 years, male had a prevalence of 2.5% as against 0.8% reported for females.

HIV status based prevalence gave 2.8% for HIV negative participants, 0.0% for those with unknown status while HIV positive had a prevalence of 0.5% (Table 3).

Assay for statistical significance reveals that age, sex and location of residence are independently associated with rifampicin resistant PTB acquisition.

By marital status, single had highest prevalence of rifampicin resistant TB 8 (2.0%) than married 5 (1.3%) due the fact that they are so much involve in socio-economic and recreational activities that predispose them to tuberculosis (TB) as shown in table 4.

Table 2 Prevalence of Rifampicin Resistance Tuberculosis PTB

Rifampicin Resistance	Frequency	Percentage (%)
Positive	13	3.3
Negative	387	96.7
Total	400	100

Table 3 Prevalence of Rifampicin Resistant PTB in Relation to Other Study

Variables	Frequency	Percentage (%)
Age Group(Years)		
10-19	32	1 (0.3)
20-29	96	3 (0.8)
30-39	93	6 (1.5)
40-49	75	2 (0.5)
50-59	56	1 (0.3)
60 and above	48	0 (0.0)
Gender		
Male	255	10 (2.5)
Female	145	3 (0.8)
HIV Status		
Positive	20	2 (0.5)
Negative	358	11 (2.8)
Unknown	22	0 (0.0)
Location of Residence		
Damaturu	127	5 (1.3)
Potiskum	114	6 (1.5)
Gashua	159	2 (0.5)

Table 4 Prevalence of Rifampicin Resistance Tuberculosis by Marital Status

Variables	Frequency	Percentage (%)
Single	67	8 (2.0)
Married	321	5 (1.3)
Divorced	12	0 (0.0)
Total	400	13 (3.3)

4 Discussion

This study confirmed the existence of RR-TB among presumptive TB patients attending DOTS clinics in Yobe State, Nigeria. Compared with the 4.3% MDR-TB cases estimated for Nigeria by (WHO 2017), the findings of this study reported lower RR-TB rate of 3.3% among the studied patients.

Other 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 GeneXpert facilities in the two areas. National update reports by NTBLCP, (2018) indicated that Lagos State had 30 GeneXpert machines while Yobe has 4 as such this variation in number of facilities could explain the difference in the rate of prevalence between the two States.

This finding is higher than that of Mohammad et al (2021) whose findings was 3.1% among presumptive TB patients in North West, Nigeria; though this could be as a result of higher sample size.

This study revealed that males had higher RR-TB prevalence than females. This observation is consistent with WHO, (2019) report that TB affects people of both sexes in all age groups but the highest burden is in men. 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).

Studies from Aminu and Tukur (2016) and southern part of Nigeria and other part of Africa showed that the prevalence of RR-TB was significantly among males (FMOHN, 2011).

Beside gender, age group and marital status are some of demographic factors that were found to be significantly associated RR-TB prevalence in the study area. Patient aged greater than > 15 years and those that are single had higher prevalence of RR-TB. The findings of this study are in agreement with (WHO, 2019; Mohammad et al. 2017; Mohammad et al, (2021) opined that this may not be unconnected with fact that patients in this age group are physically active and may be engaged in various sectors of life working experiences as such becoming more exposed to acquire and develop TB.

In a related study Adesokan, (2014), identified contact with TB patient 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 age variation that exists for the reported drug resistance rates may be a reflection of localized socio-economic factors related to exposure opportunity and MDR-TB development. Assay for statistical association between age and rifampicin resistant PTB acquisition gave a P-*value* of 0.504. Gender based prevalence gave a 2.5% (10/255) to 0.8 (3/145) ratio in favor of male gender. This is in agreement with several reports from Nigeria (Okonkwo, 2017) other parts of Africa (Coovadia, 2013) and Asia (Yang, 2014). The variation in gender-based prevalence recorded in the study may result from different in TB susceptibility, behavioral factors and degree of exposure to infection sources. Rifampicin resistance PTB acquisition or emergence status gave 0.5% 2.8% and 0.0% for HIV positive, HIV negative and those with unknown status respectively. High rates of rifampicin resistant PTB have been recorded for persons with HIV/PTB co-infection in the study which is in consonance with the record reported in Brazil, USA and Ethiopia (Jeleta, 2017). Also, the finding of this research is in contrast with record reported by (Henry *et al,* 2019) which is 5.0% (5/101) and Okonko*et al;* (2017) 4.8% (2/24) incidence for HIV/PTB Co infected participant. Their finding doesn't correlates with figures recorded in this study.

The findings of this study further indicated that, the prevalence of RR-TB is significantly associated with HIV infection because in a study, Aminu (2020) explained that the effect of HIV as witnessed among the TB patients reduces the body peripheral lymphocytes especially CD4+ which it depletion can lead to increase in the acquisition and transmission of TB.

5 Conclusion

This study confirmed the presence of rifampicin resistant TB in the study area; this remains a major public health issue. Therefore, there is a need to introduce a routine screening of presumptive TB patients in all the local government area in the state and the services should be available, affordable, and accessible to the patients who need them, so as to assist at achieving the ultimate goal of eliminating PTB as a public health issue by 2050.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflicting interests

Statement of ethical approval

The study was approved by the Yobe State Primary Healthcare l Ethical Committee (REC. 0027/2021) and confirmed consent was obtained from the each patient

Statement of informed consent

Confirmed consent was obtained from each patient.

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