Research

Prevalence of Tuberculosis, Rifampicin Resistant Tuberculosis and associated risk factors in Presumptive Tuberculosis patients attending some hospitals in Kaduna, Nigeria

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Abstract

Background: This study was carried out to determine the prevalence of Tuberculosis and *Mycobacterium tuberculosis* resistance to Rifampicin using GeneXpert in presumptive tuberculosis patients attending some hospitals in Kaduna, Nigeria.

Methods: The study design was cross sectional. A total of 198 sputum samples were collected from participants who had been administered questionnaires, and screened using Ziehl Neelsen Acid Fast Bacilli (ZN AFB) method and GeneXpert molecular technique. Data obtained from this study was analysed using the Statistical Package for the Social Sciences 23(SPSS® package version 23 Inc. Chicago Illinois, USA).

Results: Data obtained showed that using GeneXpert technique, the overall prevalence of TB and Rifampicin resistant TB (RRTB) was 40.4% and 1.25% respectively. A higher prevalence rate was reported among male subjects (47.2%), age group 31-40 (50.9%), those who earned less than 20,000 Naira monthly (41.8%), HIV positive subjects (54.5%), subjects that smoke cigarettes (72.2%) and those that had previous contact with someone living with TB infection (82.4%). The independent variables that were significantly associated with the rate of occurrence of TB ($p<0.05$ at 95% C.I) were age, gender, HIV status, smoking behaviour, and previous contact with someone having TB.

Conclusions: This study indicates high burden of TB and a low burden of rifampicin resistant tuberculosis among the participants. It highlights the need for rapid detection of TB and Rifampicin resistant strains using GeneXpert or other molecular techniques for TB diagnosis as key to early access to therapy; it will also improve treatment outcomes and decrease transmission rates.

Keywords: Tuberculosis, Rifampicin resistance, GeneXpert, Ziehl Neelsen test, Risk factors, Kaduna State

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Introduction

Background

Tuberculosis (TB) is an air borne infectious disease caused by the *Mycobacterium tuberculosis* (MTB).[1,2] It is a global health concern as it is the top cause of death from a single infectious agent, rating above Human Immunodeficiency Virus (HIV)/Acquired Immune Deficiency Syndrome (AIDS).[2,3] Tuberculosis usually affects the Pulmonary system (TB of the lungs), where it causes chronic inflammation and progressive lung damage. It can spread to other organs such as joints, liver, kidney and heart (Extra-pulmonary TB) where it causes impaired organ function and eventually death if left untreated. Transmission is mainly through inhalation of air-borne droplets produced when a person with an active infection coughs, sneezes, talks or spits. The risk of getting infected is more common in people with conditions that weaken the immune system (e.g. HIV/AIDS), or those on drugs that suppress the immune system (e.g. cancer patients, organ transplant recipients, patients with auto-immune diseases) etc. In addition, very young age, advanced age, malnutrition, tobacco smoking and alcohol use also increases the risk of TB infection.[4]

Rifampicin is by far the most effective anti-tuberculosis agent used in the care and treatment of patients with active tuberculosis.[5] It is used in combination with other anti-TB drugs such as isoniazid, ethambutol, and pyrazinamide. Rifampicin inhibits synthesis of bacterial proteins that are necessary for cellular activities by inhibiting the DNA-dependent RNA polymerase enzyme.[6] In the ensuing years, however, certain strains of Mycobacterium have emerged that have evolved resistance to common treatments through genetic alterations;[7] thus posing a critical threat to worldwide tuberculosis control. The emergence of rifampicin resistant (RR) and Multi-Drug-resistant (MDR) strains of *Mycobacterium tuberculosis* is a critical challenge to global tuberculosis control.[8,9]

In 2019, about 206,030 people were reported to have had MDR-TB globally.[2] Of the 10 million incident TB cases worldwide, 500,000 are estimated to have had rifampicin-resistant tuberculosis (RR-TB).[2,10] Studies in Nigeria reported 12.1–18.8% prevalence of rifampicin-resistant MTB.[11–14]

In 2010, WHO recommended the use of GeneXpert MTB/RIF assay, a fully automated diagnostic molecular test that simultaneously detects TB and rifampicin resistance It makes use of real-time polymerase chain reaction (RT-PCR) technology to detect specific genes for *Mycobacterium tuberculosis* in a sample (e.g. sputum) and at the same time detect mutations within the 81-base pair region of the beta subunit of bacterial RNA polymerase (rpoB) gene.[15]

Early detection of drug resistant strains offers many advantages such as prompt initiation of alternative treatment plan, reduced cost and duration of treatment, and improved patient outcomes.[2,8] This research is aimed at determining the prevalence of TB and rifampicin-resistant *Mycobacterium tuberculosis* using molecular methods as well as to identify some risk factors associated with rifampicin resistance among patients presumptive for either TB or drug resistant TB (DR TB) in Kaduna, Kaduna State, Nigeria.

Methods

Study design

The study design was cross sectional.

Study site

The study was conducted within Kaduna metropolis, Kaduna State, Nigeria. Kaduna State is in the North West geopolitical zone of Nigeria. It lies between longitudes 7°45 E and 7.75°E and latitudes 10°20 N and 10.33°N. The state is bordered by Bauchi and Plateau states to the East, Zamfara, Katsina and Kano States to the North, Nasarawa State to the South, Abuja to the South-West and to the West is Niger State. The state has a populace of above 5 million[16] and occupies 46,053 square kilometres. Kaduna city has two main local government area councils: Kaduna South and Kaduna North; nevertheless, a portion of the metropolitan spreads respectively to local government areas of Igabi and Chikun. The research was carried out in the GeneXpert laboratory of the selected facilities under study. There are just 12 GeneXpert sites in Kaduna State. These facilities receive patients from within the state as well as surrounding communities in the adjoining states.

Study Population

The study population was TB-presumptive patients (both males and females from ages one and above presenting with clinical signs and symptoms indicative of TB and patients suspected of having drug resistant tuberculosis who presented at the TB clinic unit of the St Gerard's Catholic Hospital, Kakuri, Kaduna State; General Hospital, Sabo, Sabon-Tasha Kaduna and 44

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Nigerian Army Reference Hospital Kaduna, Nigeria during the study period.

Inclusion criteria and exclusion criteria

Samples were obtained from patients known or suspected to have TB, attending clinic at St Gerard's Catholic Hospital, Kakuri, Kaduna State; General Hospital Sabo, Sabon-Tasha Kaduna and 44 Nigerian Army Reference Hospital Kaduna, Nigeria. All patients included in the study gave a signed written consent before their samples were collected. Patients infected with non-tuberculous mycobacteria (NTMs) and also those that did not consent, were excluded from the study.

Sampling methodology

The size of the sample was calculated based on 13.6% prevalence of *Mycobacterium tuberculosis* resistance to Rifampicin reported in a study conducted at National Tuberculosis and Leprosy Training Centre/Referral Hospital Zaria.[13]

The Cochran's formula for cross-sectional surveys[17] was used to calculate the sample size:

$$n = \frac{Z^2pq}{d^2}$$

Where: n= required sample size; Z = (1- α/2) = 1.96 = Z value of the standard distribution corresponding to a significance level of α (1.96 for a 2-sided test at the 0.05 level); p = Proportion or prevalence of interest (from pilot study or literature survey) expressed in percentage form= 13.6%; q = 100-p=100-13.6%=86.4%=0.864; d = clinically expected variation (precision) = 5% (0.05). Using the above information, the calculated sample size with 10% non-response rate accommodated was 198.

Data collection

The sampling technique used was a non-probability one where participants were recruited consecutively for six months until the sample size was attained. This technique was adopted due to the rare nature of the event under study, which therefore necessitated the inclusion of patients presenting primarily at the facility as well as those that came on referral. A well-structured questionnaire was administered to all participating subjects in order to obtain information on demographic data such as age, gender and HIV status.

Study variables

TB and Rifampicin-resistant *M. Tuberculosis* were the respective dependent variables while the independent variables were demographic factors such as gender, age, HIV infection status, smoking status, alcohol consumption status, income, contact with infected people and treatment-related illnesses.

Sample collection

Sputum samples were collected from all prospective patients into appropriately labelled sterile universal specimen bottles. The sputum samples were inspected for the presence of purulent material and bloodstain. The sputum samples were then taken to the laboratory for laboratory processing and analysis.

Laboratory procedures

Phenotypic detection of *M. tuberculosis* using Ziehl Neelsen staining method

The Ziehl Neelsen staining method for acid-fast bacilli was performed as described previously.[18] In brief, cooled heat-fixed smears of sputum samples prepared on microscope slides were flooded with filtered Ziehl-Neelsen 1% Carbol fuchsin solution (10g of basic fuchsin powder, 100ml of absolute alcohol, 50g of phenol crystals and 900ml of distilled water) and heated gently until vapour just began to rise. The heated stain was allowed to remain on the slide for 5 minutes and the slides were individually rinsed in a gentle flow of distilled water until all free stain was washed away. Excess water was drained off the slides by tilting the slides. The slides were then flooded with 3% acid alcohol (30ml of concentrated (hydrochloric acid) HCL and 970ml of 95% ethanol) to decolorize for 3 minutes. The smeared slides were then rinsed thoroughly with distilled water, and flooded with 0.1% methylene blue counterstain (1g of methylene blue chloride salt and 1000ml of distilled water) for 60 seconds. The stain was then rinsed off thoroughly with distilled water; the back of the slides were wiped clean, drained, air-dried and viewed under oil immersion lens using x1000 magnification alongside positive and negative control slides. Interpretation of results was done using WHO standards.[19] Presence of pinkish red rods indicated presence of acid-fast bacilli while absence of pinkish red rods indicated absence of acid-fast bacilli.

Molecular detection of *M. tuberculosis* and Rifampicin resistance using the cartridge-based nucleic acid amplification test. A cartridge-based nucleic acid amplification test namely the GeneXpert test was used to detect the presence of *M. tuberculosis* in sputum samples and identify rifampicin resistance in the clinical isolates obtained. The GeneXpert test was performed

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according to the manufacturer's protocol (Cepheid Inc., Sunnyvale, CA, USA). In brief, 1ml of sputum sample was added to 2ml of Xpert MTB/RIF proprietary NaOH and isopropanol-containing sample reagent and mixed vigorously. The mixture was incubated for 15 min at room temperature and transferred into the GeneXpert MTB/RIF Cartridge. The cartridge was loaded into a GeneXpert instrument and the software was allowed to run. The test also contains Bacillus globigii that served as an internal processing control. Samples that were negative for *M. tuberculosis* but positive for B. globigii were reported as *M. tuberculosis* negative; samples that were negative for both *M. tuberculosis* and B. globigii were identified as invalid. The test by means of polymerase chain reaction (PCR), amplifies the beta subunit of bacterial RNA polymerase (rpoB) gene. It is also capable of detecting rifampicin resistance by the failure of one or more of the rpoB-specific molecular beacons to hybridize properly to the rpoB amplicon. The test results were automatically generated as presence or absence of *M. tuberculosis*, presence or absence of rifampicin resistance in *M. tuberculosis*-positive samples.

Data analysis

Statistical Package for the Social Sciences 23 (SPSS® package version 23) was used to analyse the data gotten from this study. To describe the research participants in respect to key variables, descriptive statistics such as frequency and percentage were employed. The result of the research work was also presented in tabular forms, charts and figures. Majority of the variables were fitted to logistic regression analysis for multi-factors analysis and factors related with *M. tuberculosis* risk and rifampicin-resistance were assessed by computing the odds ratio (OR) and 95% confidence intervals (95% CI). Statistical significance level was set as <0.05.

Ethical consideration

Ethical clearance was obtained from the Ethics and Research Committee of the Kaduna State Ministry of Health and the other selected Hospitals. Permission was also obtained from the heads of TB clinics in all the selected hospitals prior to data and sample collection. Patients' privacy and confidentiality were preserved as all personal information that could link a patient to the study was removed from the study.

Results

Prevalence of TB infection

A total of 198 sputum samples were collected from consenting participants in Kaduna state and screened to detect the presence or absence of active tuberculosis infection. The result of phenotypic detection of AFB in the sputum samples using Ziehl Neelsen staining method is presented in Table 1. The test detected AFB in 65 samples (32.8%) and level of infection was quantified as scanty (2.5%), 1+ (14.1%), 2+ (11.1%), and 3+ (5.1%) according to WHO standard.[19] The test was validated by molecular detection of bacterial gene using the GeneXpert test kit. The comparison between both methods is displayed in Table 2 while the analysis of the sensitivity and specificity of both methods is shown in Table 3. Of the 133 (67.2%) participants that were screened to be free of the infection using AFB method, 15 (7.6%) were confirmed positive using the GeneXpert molecular method. This difference is statistically significant at (p= 0.0001; p<0.05)

Table 1: Prevalence of *M. tuberculosis* in clinical samples using Ziehl Neelsen staining method. Classification is according to WHO standards[19]

No of AFB	Fields	Interpretation	ZN Test (%)
No AFB seen	per 100 IF	Negative	133 (67.2)
1 – 9 AFB	per 100 IF	Positive, scanty	5 (2.5)
10 – 99 AFB	per 100 IF	Positive, 1+	28 (14.1)
1 – 10 AFB	per 50 IF	Positive, 2+	22 (11.1)
>10 AFB	per 20 IF	Positive, 3+	10 (5.1)
Total			**198 (100)**

AFB: acid-fast bacilli; ZN: Ziehl Neelsen; IF: Immersion fields

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Table 2: Comparison of *MTB* detection

Ziehl Neelsen Test	GeneXpert Test	
	Negative (%)	**Positive (%)**
Negative	118 (59.6)	15 (7.5)
Positive	0 (0.0)	65 (32.8)
Total	118 (59.6)	80 (40.4)

n = 198 sputum samples; $\chi 2 = 142.731$, df = 4, p = 0.0001 C. I = 95%, p <0.05

Table 3: Analysis of sensitivity and specificity of GeneXpert & Ziehl Neelsen result

Method	Sensitivity		Specificity	
GeneXpert Machine	True positive (+ +)	80	True Negative (- -)	118
	False Negative (+ -)	0	False Positive (- +)	0
	Sensitivity	100%	Specificity	100%
Ziehl Neelsen	True positive (+ +)	65	True Negative (- -)	118
	False Negative (+ -)	15	False Positive (- +)	0
	Sensitivity	81.3%	Specificity	100%

The result above depicts the findings of sensitivity and specificity from the screening tests of GeneXpert and Ziehl Neelsen of patients with tuberculosis. The sensitivity of the test reflects the probability that the screening test will be positive among those who have the disease. In contrast, the specificity of the test reflects the probability that the screening test will be negative among those who do not have the disease.

Thus, the sensitivity result from the GeneXpert machine suggested that a patient infected with *Mycobacterium tuberculosis* is 100% likely to test positive with tuberculosis, while the value from specificity analysis revealed that if the patient is not infected with the *Mycobacterium tuberculosis*, there is 100% probability that the test will be negative.

Comparatively the sensitivity result from the AFB ZN staining technique suggested that a patient infected with *Mycobacterium tuberculosis* is 81.3% likely to test positive with tuberculosis while the specificity result revealed that if the patient is not infected with the *Mycobacterium tuberculosis*, there is 100% likelihood that the screening test will be negative. Therefore, as shown in Figure 1 below, our findings show that the GeneXpert test is more effective than AFB ZN in screening for MTB.

Prevalence and Risk factor of TB in relation to some socio-demographic parameters

As shown in Table 4, the prevalence of TB in relation to socio-demographic parameters revealed that 108 (54.5%) males participated in this study and 51 (47.2%) showed presence of active TB infection while 29 (32.2%) females out of 90 (45.5%) had TB. TB infection was most prevalent (50.9%) among the 31-40 years age group and least (30.3%) among >40-year-olds. The investigation also shows that out of the 198 respondents that were interviewed, those that earned less than N20, 000 with frequency of 146 (73.7%) had the highest prevalence (41.8%) of MTB infection. The difference in the rate of occurrence of TB in relation to these demographic factors showed statistical significance with gender and age at 95% confidence interval. Health factors such as HIV infection, alcohol consumption, smoking and contact with someone with TB were all assessed for association with the prevalence of TB infection. Of the total test results (198), 154 (77.8%) are HIV negative subjects while 44 (22.2%) are HIV positive subjects. Out of these 44 HIV positive subjects, 24 (54.5%) were infected with MTB. There was significant association between TB and HIV status at (OR =2.749, 95% CI: 1.192 – 6.340, p=0.018), this implies that a subject infected with HIV is 2.749 times more likely to have TB than a subject without HIV.

The relationship between TB prevalence and alcohol consumption showed no association (p=0.061). Out of

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the 37 participants that take alcoholic substances, 13 (35.1%) were MTB positive while out of the 161 respondents that do not take alcoholic substances, 67 (41.6%) were MTB positive.

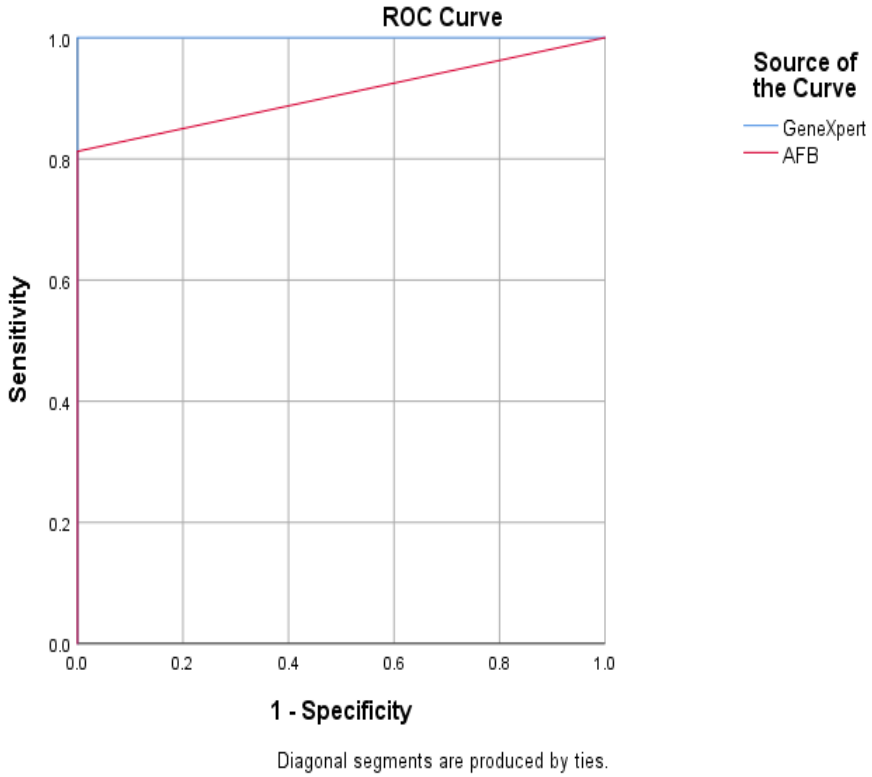

Fig 1: Sensitivity Analysis for Tuberculosis screening with GeneXpert and AFB method

Cigarette smoking was found to be associated with the prevalence of TB in this study (OR =7.077, 95% CI: 1.861–26.923, p=0.004), suggesting that cigarette smoking is risk for TB disease. By implication the likelihood of having TB is 7.077 times higher for subjects who smoke cigarette than in subjects who do not smoke cigarette. Of the 198 participants, 180 (90.9%) do not smoke cigarettes while 18 (9.1%) do smoke cigarettes. Of these 180 participants that do not smoke, 67 (37.2%) were MTB positive while of the 18 that smoke, 13 (72.2%) were MTB positive.

Also, living with someone that has TB infection showed a statistically significant association with the prevalence of TB (OR =12.770, 95% CI: 5.322–30.639, p=0.0001), this connotes that subject who had contact with person with TB disease is 12.770 times more likely to have TB than subject who had no contact with TB patients. From the 198 participants, 51 (25.8%) had lived with someone with TB from which 42 (82.4%) were TB positive, 147 (74.2%) had not lived with someone with TB from which 38 (25.9%) were TB positive.

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Table 4: Prevalence of TB in relation to associated risk factors using Logistic Regression

Variables	Frequency (%)	*MTB* Not Detected (%)	*MTB* Detected (%)	p-value	OR (95% Confidence Interval)
Gender					
Male	108 (54.5)	57 (52.8)	51 (47.2)	0.049**	2.106 (1.003 – 4.419)
Female	90 (45.5)	61 (67.8)	29 (32.2)		
Age (years)					
1 – 1 0	2 (1.0)	1 (50.0)	1 (50.0)	0.046**	2.191 (1.013 – 4.738)
11 - 20	24 (12.1)	16 (66.7)	8 (33.3)		
21 – 30	51 (25.8)	28 (54.9)	23 (45.1)		
31 - 40	55 (27.8)	27 (49.1)	28 (50.9)		
>40	66 (33.3)	46 (69.7)	20 (30.3)		
Income (in Naira (N))					
<N20,000	146 (73.7)	85 (58.2)	61 (41.8)	0.514	1.299 (0.593 – 2.846)
>N20,000	52 (26.3)	33 (63.5)	19 (36.5)		
HIV status					
Positive	44 (22.2)	20 (45.5)	24 (54.5)	0.018**	2.749 (1.192 – 6.340)
Negative	154 (77.8)	98 (63.6)	56 (36.4)		
Alcohol consumption					
YES	37 (18.7)	24 (64.9)	13 (35.1)	0.165	0.490 (0.179 – 1.341)
NO	161 (81.3)	94 (53.4)	67 (41.6)		
Cigarette smoking					
YES	18 (9.1)	5 (27.8)	13 (72.2)	0.004**	7.077 (1.861 – 26.923)
NO	180 (90.9)	113 (62.8)	67 (37.2)		
Contact with persons with TB					
YES	51 (25.8)	9 (17.6)	42 (82.4)	0.0001**	12.770 (5.322 – 30.639)
NO	147 (74.2)	109 (74.1)	38 (25.9)		
Total	**198 (100.0)**	**118 (59.6)**	**80 (40.4)**		

Factors with ** p-values are 5% statistically significant

Prevalence of rifampicin-resistant Mycobacterium tuberculosis in clinical samples

Mutations within the 81-base pair region of the rpoB gene were investigated via GeneXpert methods. The result showed that out of the 80 (40.40%) sputum samples that were positive for *MTB*, only 1 (1.25%) was rifampicin (RIF) resistant (Fig. 2).

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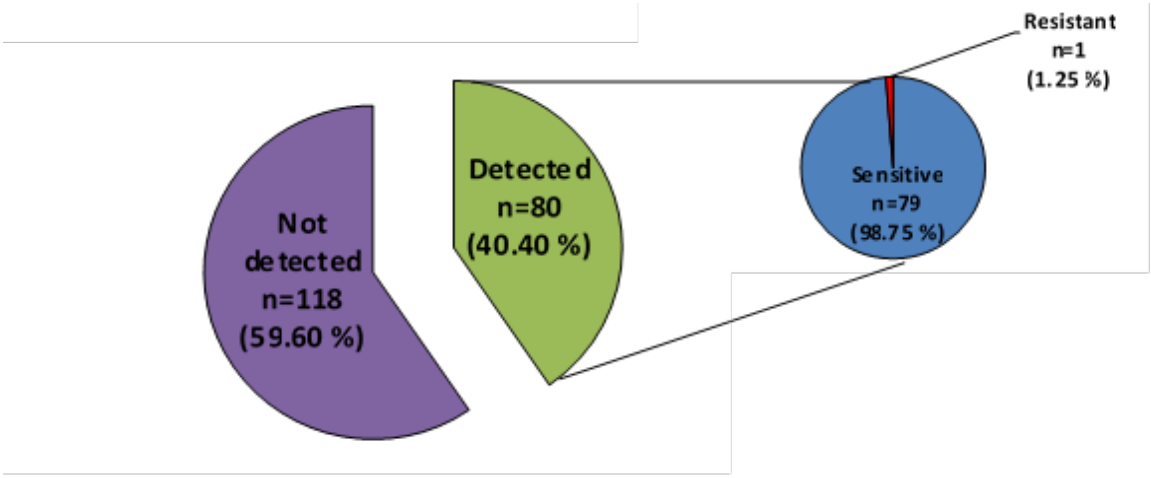

Fig. 2: Prevalence of TB infection and rifampicin-resistant isolates

Percentage distribution of some health care related factors that might be associated with TB infection. Out of the 49 (24.7%) participants that had previous history of TB, 14 (28.6%) did not adhere to treatment, 2 (4.1%) were not enlightened on the duration of treatment and 3 (6.1%) were not informed by the health care providers on the need for adherence to drug treatment.

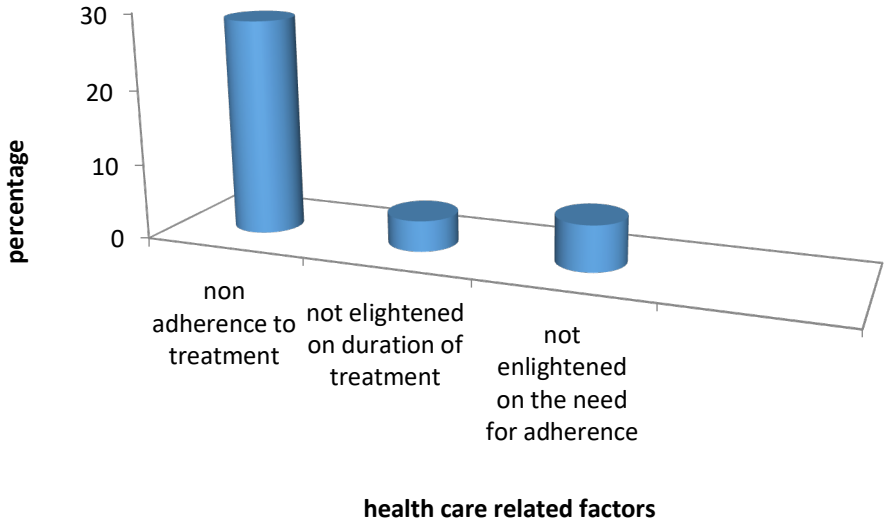

Fig. 3: Percentage distribution of some health care related factors that might be associated with TB infection

Discussion

This study recorded an overall prevalence of TB infection and Rifampicin resistance as 40.4% and 1.25% respectively using GeneXpert method.

The prevalence of TB infection recorded in this study is similar to 35.6%, 31.4% and 37% reported from Akure, Nigeria,[12] Lagos and Jos, Nigeria[20] and Pakistan[21] respectively. However, it was lower compared to reports

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from Zaria (88.6%)[22] and Saye Zaria (40.5%).[13] In contrast, our study showed a higher prevalence than studies conducted in Borno (19.1%),[23] Makurdi (25.5%),[24] Ogun (16.7%),[25] Calabar (24.8%)[26] and Ethiopia (23.2%).[27] These differences might be due to difference in the methods used for detection of *M. tuberculosis,* the nature and type of subjects included in the study, the hospital used (Special *MTB* Referral hospitals, DOTs Centres etc), degree of endemicity of Tuberculosis infection and the geographical area where the study population was located.

Age group of 31 – 40 years had the highest proportion of GeneXpert positive *MTB* cases (50.9%), this data is statistically significant. This finding is in tandem with previous reports in Kano[28] and Ogun State.[25] Tuberculosis affects adults generally in their prime working age.[4] Exposure to risks factors such as indiscriminate sexual acts by this sexually active reproductive age group, imprisonment, smoking and migration, which is more common among this economically productive age group, might be another reason. This study was however contrary to another report in Nigeria that showed that TB infection was higher in age group 40years and above.[29]

The prevalence of *TB* was significantly higher in males (47.2%) than females (32.2%). Reports from Ogun,[25] Ethiopia[27] and WHO[2] support this finding. The reason for this could be because males are more involved in interacting with the outer environment due to work activities and travelling and as such are more liable to inhalation of the bacilli from the environment than the female counterparts Another reason for this gender bias may be the effect of sex hormones and genes linked to the X chromosome, on the immune system.[30] Females have higher resistance to microbial infections in humans, implying that females have a more robust immunological defence against most invading pathogens.[31] Oestrogen stimulates the immune system, whereas testosterone suppresses it.[32] Testosterone has also been proven to inhibit the immune system by upregulating anti-inflammatory cytokines (IL-10), whilst oestrogen boosts the immune system by upregulation of pro-inflammatory cytokines. (TNFα).[30] Despite the fact that majority of studies are in line with this finding. In a particular study, it was reported that more females were infected with TB.[33]

Human Immunodeficiency Virus (HIV) comorbidity is a confounder factor for the TB diagnosis.[1] In our study, the rate of HIV/TB co-infection was 54.5% and this coinfection is found to be statistically significant. Out of the total 198 respondents, the rate of HIV/TB co-infection was 12.1% (24 out of 198); this is in accordance with reports from Nigeria where the TB prevalence among HIV Clients at Global Fund supported facilities by zone and state was studied and TB/HIV coinfection prevalence for Kaduna state were found to be 8.2% from January to June, 2015 [34] Similar rate of 9.5% has also been reported in Edo State.[35] It was observed from this study that the risk of developing TB is 2.749 times greater in people living with HIV than among those without HIV infection. According to WHO,[4] the risk of developing TB is 16-27 times greater in people living with HIV than among those without HIV infection. A higher prevalence of 16.6% and 22.2% were reported in studies carried out in Ethiopia[27] and Makurdi, Benue state[24] respectively. A much lower rate of 1.9% was however reported in Saudi Arabia by.[36] Variations in this data may be due to the epidermicity of HIV infection in the locations and also the study population. Tuberculosis is a major health risk, particularly for those individuals living with HIV, due to the fact that their immune system is compromised. TB is one of the top causes of mortality among HIV-positive persons globally.

Furthermore, this study also confirmed that using GeneXpert for the detection of TB was more sensitive and had more diagnostic yield than AFB Ziehl Neelsen smear microscopy method. Our findings showed that 133 (67.2%) samples tested were AFB smear negative, but GeneXpert was able to detect the presence of *MTB* in 15 (7.6%) smear negative sputum samples scaling down those with true negative results to 118 (59.6%). Majority of the cases that went undetected by smear microscopy were from patients with TB/HIV coinfection. This result is congruent with the findings of a comparative study of GeneXpert with Ziehl Neelsen stain in samples of probable pulmonary TB patients (37) where the sensitivity of GeneXpert in sputum assay was found to be 100%. This is because even low *MTB* genomic copies in various specimens can be detected and as such, has the ability to profoundly improve tuberculosis case detection in areas where conventional diagnostics have been woefully inadequate especially in people with suspected HIV-associated TB with very low *MTB* genomic copies.[38]

People with immune systems that are compromised, such as smokers, have an increased risk of contracting TB infection and falling ill.[4] It was discovered from this

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study that 6.6% out of the 9.1% participants that smoke cigarette were infected with *MTB*. Thus, significantly relating smoking to be a factor that increases the risk of contracting TB. This agrees with research carried out in Nigeria,[26,39] Korea,[40] and South Africa[41] where it was discovered that smoking was linked to an increased risk of both incidence and recurrence of TB infection. This relationship is likely because smoking has a wide range of consequences on pulmonary structure and function and has an effect on host defenses both in the lung and throughout the body system thereby affecting the immune system and making people more susceptible to TB disease.[42] It was observed from the study that the participants who smoked were 7.077 times more likely to be TB infected than participants who do not smoke.

The relationship between TB infection and income earned was also shown in this study. Participants who earned less than 20,000 naira in a month had the highest prevalence (41.8%) of TB infection. This just further buttresses the fact that TB infection is more common among people with low income.[43]

This study further revealed the relationship between developing TB infection and previous contact with someone infected with TB. This was found to be statistically significant and therefore corroborates the findings that people with active TB can infect 5–15 other people through close contact over the course of a year.[4] This is also in agreement with previous reports from Croatia[44] and Ibadan, Nigeria.[45] These reports indicated that contact with TB patients was a significant behavioural factor for TB transmission.

From this present study, it was discovered that the difference in the rate of occurrence of TB in relation to whether the respondents consumed alcoholic drinks or not, is however not statistically significant Out of the 37 respondents that consumed alcoholic substances, 13 (35.1%) were *MTB* positive. This contradicts research that found alcohol intake to be a major risk factor for TB, most especially heavy use of more than 40g of ethanol per day, which resulted in a roughly three-fold increase in TB risk.[46] The reason for this variation may be because participants who consumed alcohol in this study were not heavy consumers.

This study recorded overall prevalence of Rifampicin resistant TB in the three hospitals studied in Kaduna State at 1(1.25%). This finding was similar to the work that reported 2% in Lagos state[47] and 4.2% from a study on the prevalence of Rifampicin resistant TB among patients that have been previously treated for pulmonary TB in Nigeria's North western region.[48] This data is also congruent with the Global TB reports by WHO in 2016, which show low levels of MDR/RRTB (< 3%) in new TB patients in various regions globally.[43] The overall findings is however lower than 6.1% cases in Borno State Nigeria[23] and 7.3% in Delta State.[49] Much higher prevalence of 49.1%, 18.8%, 13.6% , 14.7% and 29.4% were however found in other studies in India, Yenagoa, Saye Zaria, Akure and Makurdi respectively.[12,13,24,50,51] The difference in the various prevalence rate could be traced to the extent and burden of MDRTB/RRTB in the geographical location, test methods used, sample size, poor record and data keeping. Anti-TB drugs exposure, treatment practices and implementation of national control programmes could be issues also.[52]

Furthermore, the RRTB case detected has had a previous contact with someone living with TB infection. This implies that the participant directly contracted the Rifampicin resistant strain. Transmitted or primary drug resistant TB results from the direct transmission of drug resistant *MTB* strain from one person to another.[3] It was previously thought that the majority of drug-resistant tuberculosis was caused by acquired tuberculosis. Researchers have been able to explore this deeper due to the use of modern techniques, and they have discovered that primary resistance has a far greater role in resistance than previously assumed.[3]

Implications of the study findings

Findings from this study should provide critical patient management decisions regarding treatment and successful patient outcomes, help planning of effective public health control measures and provide information for data-based decision making and adequate planning for infection control by the facility management and National TB control. Identification and documentation of high-risk group from this study, go a long way in the planning of effective public health control measures.

Strengths and limitations of the study

The strengths of this study include the diversity of the age range covered as both young and old were included in the study as well as the considerably high number of independent variables used.

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This study also had some limitations which include difficulty in obtaining ethical approval delayed the early completion of the work as well as the accuracy of the responses generated depended on the accuracy of information given by the respondents.

Conclusion

The prevalence of Rifampicin resistant TB reported in the study may be lower compared to other reports but it still stands that even the lowest prevalence rates of MDR-PTB remains a major public health issue. GeneXpert was also confirmed to be more sensitive in the early detection of TB and Rifampicin resistant TB. Furthermore, a statistical association ($p<0.05$) exists between TB infection and age, gender, HIV infection, cigarette smoking and contact with someone having TB infection. No statistical difference was observed between TB infection and alcohol consumption, and income. Previous contact with someone who has been infected with the resistant strain of *MTB* was associated with acquisition of rifampicin resistance.

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