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Full Length Research Article

GENE-XPERT DETECTION OF MYCOBACTERIUM TUBERCULOSIS AMONG PATIENTS WITH SUSPECTED CASES OF PULMONARY TUBERCULOSIS IN NATIONAL TUBERCULOSIS AND LEPROSY TRAINING CENTER AND REFERRAL HOSPITAL, SAYE–ZARIA, NIGERIA

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ABSTRACT
Mycobacterium tuberculosis, the causative agent of tuberculosis, is one of the most ancient chronic infectious illnesses and the second greatest cause of infectious death worldwide, behind COVID-19. This study was conducted at the National Tuberculosis and Leprosy Training Center and Referral Hospital, Saye, Zaria, Nigeria, with the intention of detecting *Mycobacterium tuberculosis* among patients with suspected cases of pulmonary tuberculosis. Gene-Xpert MTB/RIF assay was employed in detecting *Mycobacterium tuberculosis* (MTB) and multi-drug resistant MTB. Thirty three (23.0%) of the 100 sputum samples obtained were positive for *Mycobacterium tuberculosis*. Two (8.7%) of the 23 *Mycobacterium tuberculosis* were found to be MDR-MTB, while the remaining 21 (91.3%) were not. The study found that there were statistically significant differences in the age-based distribution of *Mycobacterium tuberculosis* infection among the patients. Specifically, patients aged 2-25 years old had the highest rate of *Mycobacterium tuberculosis* infection (33.3%), while patients aged 49-71 years old had the lowest rate (3.8%). The male patient population had a slightly higher prevalence of 23.1% than the female patient population of 22.9%, although the difference was not statistically significant (P=0.985). Based on the patients' marital status, there was a statistically significant (P = 0.003) difference in the infection distribution; the prevalence of the infection was higher in single (i.e., unmarried) patients—38.5%—than in married patients (13.1%). Malnutrition (P=0.000), cattle rearing (P=0.026, OR=4.028), and a history of tuberculosis (OR=1.362) are additional significant risk factors. Health facilities should use the GeneXpert assay to quickly diagnose tuberculosis and identify cases of multi-drug resistant TB. This will enable a more efficient and timely course of treatment.

Keywords: Gene-Xpert MTB/RIF assay; Pulmonary Tuberculosis; *Mycobacterium tuberculosis;* Prevalence; MDR-TB.

INTRODUCTION
After COVID-19, tuberculosis is the second most common infectious killer and the thirteenth largest cause of overall death (WHO, 2021). One of the earliest chronic infectious diseases known to science, it is brought on by the single infectious agent *Mycobacterium tuberculosis* (WHO, 2020). The infection known as pulmonary tuberculosis (pulmonary TB) is caused by inhaling droplet nuclei containing *Mycobacterium tuberculosis* organisms. However, tuberculosis infection (extra-pulmonary TB) can also affect other sites. Inhaling less than 10 bacilli can result in the spread of a new infection due to the extremely low infection dose of *M. tuberculosis* (Parija, 2012; WHO, 2021). Pulmonary TB is the most prevalent type and is easily disseminated by aerosol droplets. There is a very high probability that someone else will become infected if they breathe in air containing these droplet nuclei. Delays in disease diagnosis and treatment initiation raise the risk of transmissibility (William *et al.,* 2015).

The number of cases of tuberculosis that were newly diagnosed and reported decreased significantly worldwide, from 7.1 million in 2019 to 5.8 million in 2020. Nonetheless, the death rate has gone up due to decreased access to diagnosis and treatment. The number of estimated tuberculosis deaths among HIV-negative individuals rose from 1.2 million in 2019 to 1.3 million in 2020. Additionally, it was estimated that 209,000 HIV-positive patients died from tuberculosis in 2019; this number rose to 214,000 in 2020 (WHO, 2019; WHO, 2021). Africa is estimated to account for 25% of all TB cases currently in existence and 34% of related deaths globally in 2019 (Sullivan *et al.,* 2017). Access to crucial TB diagnostics, care, and treatment services is severely restricted in this region (Tiamiyu *et al.,* 2020). The detrimental effects of tuberculosis are more noticeable in low- and middle-income nations (WHO, 2024). With almost 2.5 million cases and 424 000 fatalities from a single infectious agent in Africa in 2022, tuberculosis (TB) was the second most common cause of death in the continent (Olaleye *et al.,* 2023). Together with its population, Nigeria is experiencing an increase in tuberculosis cases. Nigeria, for instance, has the sixth-highest TB burden in the world, with an estimated 4.3% of new cases exhibiting multi-drug resistance (WHO, 2010).

Because HIV-associated tuberculosis and multidrug-resistant tuberculosis (MDR-TB) were two of the factors affecting the epidemic in previous years, TB prevention, diagnosis, and treatment were more difficult. Due to delayed diagnosis and the inability of conventional diagnostics to significantly reduce transmission, TB kills a lot of people. Chest radiography, smear microscopy, and culture are the traditional techniques for TB detection (Barnes, *et al.,* 1991). They cannot identify drug resistance and can only be used to diagnose tuberculosis in cases where sputum has a high enough bacillary load. Sputum smear microscopy has several important limitations. Persons living with HIV (PLHIV), particularly those experiencing severe

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immunosuppression, typically have very low numbers of bacilli, HIV-associated TB thus frequently remains undiagnosed (Amy *et al.,* 2013). Each year, the problems associated with drug-resistant tuberculosis (DR-TB) result in millions of cases of illness and death (Sullivan *et al.,* 2017). Xpert MTB/RIF® (or Xpert) provides a significant advancement over these constraints (Dye and Williams, 2008).

The Gene-Xpert MTB/RIF assay, which uses a nucleic acid amplification technique to detect *Mycobacterium tuberculosis* (MTB) and resistance to rifampicin within about two hours, has been endorsed by the WHO for the rapid detection of MDR-TB (Dye and Williams 2008). For the detection of tuberculosis and drug resistance testing, more advanced diagnostic instruments that are both affordable and effective must be used (WHO, 2014; Fadeyi, *et al.,* 2017).

In this study, in order to quickly and accurately diagnose MDR-TB in patients with suspected cases of pulmonary tuberculosis at the National Tuberculosis and Leprosy Training Center and Referral Hospital, Saye-Zaria, Nigeria, the Gene-Xpert MTB/RIF assay was used.

METHODS

Study Area

The National Tuberculosis and Leprosy Training Centre (NTBLC) in Saye-Zaria, Nigeria, was the site of the study.

Sample Size and Population

Our sample size, $n = Z^2p(1 - p)/w^2$, was determined using Fisher's formula, where P (prior prevalence of MDR-TB) = 4.2% (Helb *et al.,* 2010), Z (standard deviation [SD] at 95% confidence interval) = 1.96, W (degree of accuracy) = 0.05, and 1 – p = 0958 (inclusive). n = 61.8, $n = 1.96^2$ (0.042 [0.958]/0.05^2). The sample size calculation was rounded to the nearest hundred, though. Patients (male and female) with suspected cases of pulmonary tuberculosis, of all ages, attending the National Tuberculosis and Leprosy Training Centre and Referral Hospital, Saye-Zaria, were the source of the samples.

Ethical Approval

The National Tuberculosis and Leprosy Training Centre and Referral Hospital's ethical committee in Saye-Zaria, Nigeria, granted ethical approval (assigned number: NHREC/10/05/2024).

Questionnaire Administration

Prior to sample collection, a questionnaire was used to obtain information on risk as well as socio-demographic factors from the patients.

Sputum Collection and Analysis

For the purpose of the study, a total of 100 patients with pulmonary tuberculosis who were clinically suspected were enrolled. Every participant had a specimen of sputum taken. The GeneXpert MTB/RIF® was used to analyze the collected sputum specimens in order to identify *M. tuberculosis* infection and its susceptibility to RIF. In summary, the sputum sample was liquefied by mixing 1.0 ml of it with 2.0 ml of buffer, and the mixture was then incubated at room temperature for 15 minutes inside a closed tube. Throughout the 15-minute incubation period, the closed tube was manually shaken twice. After that, 2.0 ml of the diluted sample was added to the cartridge so that the Mycobacteria could be lysed ultrasonically to release the target DNA. To continue with the remainder of the protocol, the cartridge was placed into the GeneXpert device (Cepheid). The comprehensive test result was displayed on a computer screen and prepared for printing after one and a half hours.

Statistical Analysis

Data obtained from the computer printout and questionnaires were subjected to Chi Square (χ^2) and Odds Ratio (OR) analyses at 95% confidence interval on IBM SPSS version 20. Those factors that had statistical p-value ≤ 0.05 were considered significant. Final results were simplified using a chart and tables.

RESULTS

Out of the 100 patients suspected with pulmonary tuberculosis, between the ages of 2-71 years old which comprised of 48 females and 52 males, the overall prevalence of *Mycobacterium tuberculosis* infection among them was 23.0%; while 77.0% were negative (Figure 1).

Out of the 23 *Mycobacterium tuberculosis* detected, 2 (8.7%) were MDR-TB while 21 (91.3%) were non MDR-TB (Figure 2).

Patients between the age group of 2-25 years had the highest rate of *Mycobacterium tuberculosis* infection (33.3%), followed by 26.3% infection among those between 26-48 years old; while the least infection was 3.8% which was recorded among patients between 49-71 years. Differences in age-based distribution of *Mycobacterium tuberculosis* infection among the patients was statistically significant (P = 0.020) as shown in Table 1.

Also in Table 1, *Mycobacterium tuberculosis* infection of 23.1% among the male patients was only slightly higher than 22.9% among the females, which was not statistically significant (P = 0.985). However, the female patients had an identified higher risk of the infection (OR = 1.009).

Socio-economic distribution of *Mycobacterium tuberculosis* infection among the patients is presented in Table 2. Those patients that were single (i.e., not married) had prevalence of 38.5% of the infection, which was higher than 13.1% among other patients that were married. The distribution of the infection varied statistically significantly (P = 0.003) according to the patients' marital status. Married individuals, however, had a higher risk of contracting the infection (OR = 4.141).

Patients who had completed tertiary education had the highest rate of *Mycobacterium tuberculosis* infection (31.6%), followed by those who had completed primary education (23.5%) and informal education (20.7%); patients who had completed secondary education had the lowest rate of infection (20.0%). Table 2 indicates that the statistical difference in the infection distribution according to their educational attainment was not significant (P = 0.787).

Based on the patients' occupations (Table 2), the unemployed had the highest rate of *Mycobacterium tuberculosis* infection (30.6%), while those in business ventures had the lowest rate of infection (21.1%), and farmers had the lowest rate of infection (15.4%). P = 0.351 indicates that occupation had no significant impact on the infection distribution among the study's patients.

Patients with urban residences had a higher infection rate of Mycobacterium tuberculosis (25.6%) compared to those with rural residences (21.3%). Based on the patients' residential areas, there was no statistically significant difference in the incidence of

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infection (P=0.616). However, Table 2 shows that patients from rural areas had a higher risk of infection (OR = 1.273).

A few risk factors for Mycobacterium tuberculosis among the patients are shown in Table 3. Patients who worked in healthcare had a higher infection rate—33.3%—than patients who weren't in the industry, who had a lower infection rate—22.7%. P = 0.666 indicates that there was not a significant difference. Infection rates were higher in patients receiving chemotherapy (28.9%), smoking cigarettes (50.0%), or having close contact with an infected person than in patients not receiving chemotherapy (P>0.05). However, among the patients, a history of tuberculosis (OR = 1.362), malnutrition (P = 0.000), and cattle rearing (P = 0.026, OR = 4.028) were found to be significant risk factors for Mycobacterium tuberculosis infection

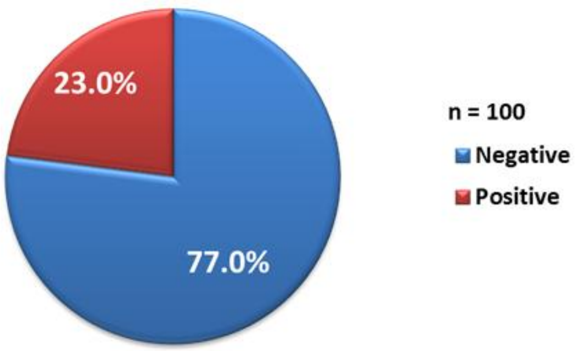

Figure 1: Overall Prevalence of *Mycobacterium tuberculosis*

Key: n = Number of Sample Collected

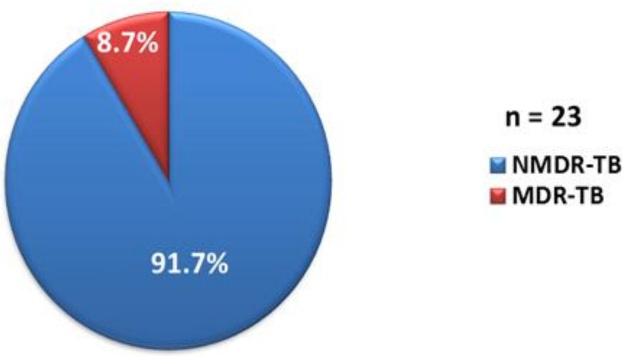

Fig. 2: Occurrence of Multi-Drug Resistance TB among Detected *Mycobacterium tuberculosis*

Key: n = Number of Detected *mycobacterium tuberculosis*; NMDR = Non Multi-Drug Resistant; MDR = Multi-Drug Resistant

Table 1: Age and Gender-Based Distribution of *Mycobacterium tuberculosis* Infection

Factor	Number examined	*Mycobacterium tuberculosis* Number positive (%)	χ^2	df	P-value	OR
Age (years)						
2-25	36	12(33.3)	7.792	2	0.020	n.a
26-48	38	10(26.3)				
49-71	26	1(3.8)				
Gender						
Female	48	11(22.9)	0.000	1	0.985	1.009
Male	52	12(23.1)				0.991

Key: n = Not applicable

Table 2: The Socio-Economic Factors that Influence the Distribution of *Mycobacterium tuberculosis* Infection among the Patients

Socio-Economic Factor	Number Examined	*Mycobacterium tuberculosis* Number Positive (%)	χ^2	df	P-value	OR
Marital Status						
Married	61	8(13.1)	8.630	1	0.003	4.141
Single	39	15(38.5)				0.242
Educational Level						
Informal	29	6(20.7)	1.058	3	0.787	n.a
Primary	17	4(23.5)				
Secondary	35	7(20.0)				
Tertiary	19	6(31.6)				
Occupation						
Business	38	8(21.1)	2.093	2	0.351	n.a
Farmer	26	4(15.4)				
Unemployed	36	11(30.6)				
Residence						
Rural	61	13(21.3)	0.252	1	0.616	1.273
Urban	39	10(25.6)				0.785

Key: n = Not applicable.

Table 3: Prevalence of *Mycobacterium tuberculosis* Infection among Patients based on Risk Factors

Risk factors factor	Number examined	*Mycobacterium tuberculosis* Number positive (%)	χ^2	df	P-value	OR
History of tuberculosis						
No	69	17(24.6)	0.337	1	0.562	0.734
Yes	31	6(19.4)				1.362
HIV status						
Negative	99	23(23.2)	0.302	1	0.583	n.a
Positive	1	0(0.0)				
Health worker						
No	97	22(22.7)	0.186	1	0.666	1.705
Yes	3	1(33.3)				0.587
Cattle rearing						
No	68	20(29.4)	4.933	1	0.026	0.248
Yes	32	3(9.4)				4.028
Malnutrition						
No	33	0(0.0)	14.712	1	0.000	n.a
Yes	67	23(34.3)				
Placed on chemotherapy						
No	55	10(18.2)	1.602	1	0.206	1.828
Yes	45	13(28.9)				0.547
Cigarette smoking						
No	92	19(20.7)	3.579	1	0.059	3.842
Yes	8	4(50.0)				0.260
Contact with infected individual(s)						
No	88	19(21.6)	0.822	1	0.365	1.816
Yes	12	4(33.3)				0.551

Key: n = Not applicable

DISCUSSION

In this study, patients with suspected cases of pulmonary tuberculosis at the National Tuberculosis and Leprosy Training Center and Referral Hospital, Saye–Zaria, Nigeria, were tested for *Mycobacterium tuberculosis* and MDR-TB using the Gene-Xpert MTB/RIF Assay. DNA from the Mycobacterium tuberculosis (MTB) complex and mutations linked to rifampicin (RIF) resistance can be detected by the assay at the same time. It is a trustworthy stand-in for sputum specimens that can identify MDR-TB in less than two hours (Kennethe *et al.,* 2021). The overall prevalence of TB among the 100 recruited patients in this study was 23%. As per a report, Africa was responsible for 23% of all tuberculosis cases worldwide (WHO, 2024). This is consistent with our findings, even though the WHO's coverage was broader and our sample area was restricted to a hospital. The rate was more in line with the 21.3% recorded in Enugu, Nigeria (Kennethe *et al.,* 2021). But it was higher than the 12.0% and 18.0% reported in the Indian state of Puducherry (Ramachandra *et al.,* 2024) and Southwest Ethiopia (Abayneh and Teressa, 2022) respectively. Variations in study participants, study period, sample size, sampling technique, geographic location, and tuberculosis control and prevention practices could be the cause of the differences.

Occurrence of rifampicin-resistant TB among the detected *Mycobacterium tuberculosis* was 8.7% which was lower to the 13.6%, 23.4% and 14.3% previously reported elsewhere in Nigeria (Fadeyi *et al.,* 2017; Adejumo *et al.,* 2018; Kennethe *et al.,* 2021). This implies improve in avoidance of drug abuse and self-medication. There was also 61.41% reported case of MDR-TB in a study on “Gender and Drug-Resistant Tuberculosis in Nigeria” (Oladimeji *et al.,* 2023). The large disparity here may be because of the differences larger sample size and cover area in the previous study, as the study covered the entire Nation. However, it was higher than the 5.7% reported in Southwest Ethiopia (Abayneh and Teressa, 2022).

Differences in age-based distribution of *Mycobacterium tuberculosis* infection observed here was statistically significant (*P* = 0.020). Patients between the ages of 2-25 years old had the

 https://dx.doi.org/10.4314/swj.v20i1.57

highest prevalence of *Mycobacterium tuberculosis* infection of 33.3%, followed by 26.3% infection rate among those between 26-48 years old; while the least infection was 3.8%, which was recorded among patients between 49-71 years old. A population-based study in Viet Nam showed that 36.8% of $\geq$ 15 years age group was infected with TB (Marks *et al.,* 2018). The similarity is compared to the one we observed among our 2-25 years age group. Comparing the age group 2–25 years in our study to the previous report, the age group 15–24 years had a lower prevalence of tuberculosis (13.3%) (Sriram *et al.,* 2023). Compared to Sriram *et al*. study, (2023) which found that older patients had a higher incidence of TB infections; our study's older patient infection rate was lower. Additionally, there was a report on correlation between age and an increased risk of tuberculosis infection (those aged 70–74 had a 2-3 times higher rate of infection than those aged 20–24) (Dong *et al.,* 2022). These results ran counter to what we found.

Male patients had a slightly higher *Mycobacterium tuberculosis* infection rate (23.1%) than female patients (22.9%). Reports of Lienhardt et al. (2003), Mulu *et al.* (2017), Saeed et al. (2017), Enos *et al*. (2018), and Diriba and Churiso (2022) from developing nations corroborate the rate, which was not statistically significant (P = 0.985). There was also a report of a higher *M. tuberculosis* rate among male patients in Ethiopia (Araya *et al.,* 2020). There's a chance that the results of this study are linked to men's increased exposure to crowded places and to behaviors, like drinking and smoking. The female patients, however, were found to be at a higher risk of infection (OR = 1.009).

Patients without a partner (i.e. not married) had an infection rate of 38.5%, higher than the infection rate of 13.1% among patients who were married. A higher rate of tuberculosis (TB) was previously observed in unmarried patients (48.0%) as opposed to married patients (46.0%) (Lienhardt *et al.,* 2005). This was unsurprising, as single individuals (those without a spouse) tend to be mobile and frequently relocate, living alone or with friends, increasing their susceptibility to tuberculosis infections. Living alone and being single was a risk factor for tuberculosis on its own (Gustafson *et al.,* 2004). The distribution of the infection was statistically significantly (P = 0.003) among the patients in our study according to their marital status. Nonetheless, patients who were married had a higher infection risk (OR = 4.141) than patients who were single.

In the present investigation, patients with tertiary education had the highest rate of pulmonary *Mycobacterium tuberculosis* infection (31.6%), followed by primary and informal education (23.5% and 19.7%), and secondary education (20.0%) patients with the lowest infection rates. Our results here were in conflict with a report that claimed patients with secondary education had a higher rate of pulmonary *Mycobacterium tuberculosis* infection (42.17%) than patients with PG (1.42%) and Graduate (6.55%) levels of education (Imam et al., 2021). Nonetheless, P value = 0.787 indicates that the variation in infection distribution according to educational attainment in our investigation was not statistically significant. The findings of a prior study, which found no connection between educational attainment and the incidence of pulmonary tuberculosis infection, were in line with the findings of this investigation regarding the educational attainment in relation to contracting *Mycobacterium tuberculosis* (Rusnoto et al., 2019).

In our study, occupation and residency were additional socioeconomic factors that did not significantly correlate with the acquisition of pulmonary tuberculosis. However, the highest rate of pulmonary *Mycobacterium tuberculosis* infection was found in the unemployed (30.6%), compared to 21.1% among those in business ventures; the lowest rate of infection was found in farmers (15.4%). Patients living in urban areas had a higher prevalence of pulmonary *Mycobacterium tuberculosis* infection (25.6%) compared to patients living in rural areas (21.3%), and patients in rural areas had a higher infection risk(OR = 1.273).

Patients who worked in the medical field had a higher infection rate of 33.3% than non-workers, who had a lower infection rate of 22.7%. P = 0.666 indicates that there was no significant difference.

Patients receiving chemotherapy had an infection rate that was higher (28.9%) than that of patients who were not receiving it (18.2%). This result was consistent with a report that found that patients receiving chemotherapy had a 13.0% TB infection rate, compared to a 3.9% infection rate for patients not receiving chemotherapy (Aldabbagh et al., 2022). Chemotherapy lowers the number of white blood cells and weakens immune responses by affecting many normal dividing tissues, including the bone marrow (Breastcancer,2022). Patients in this group are susceptible to tuberculosis activation. Patients receiving chemotherapy may have a higher infection rate as a result of the treatment. On the other hand, P>0.05 indicates that there was no significant correlation between the infection rate and chemotherapy.

According to our research, the prevalence of tuberculosis was higher in tobacco smokers (50.0%) than in non-smokers (20.7%). P value = 0.059, however, indicated that there was no significant correlation between the infection and tobacco use. This went against reports that linked tobacco use to a higher risk of tuberculosis (Lin et al., 2007; Slama et al., 2007).

Malnutrition was substantially associated with the infection (P=0.000) among the 67 malnourished patients in our study, of whom 34.3% tested positive for tuberculosis. A secondary immunodeficiency brought on by malnutrition has been linked to an increased susceptibility of the host to infections, including *Mycobacterium tuberculosis* (Gupta *et al.,* 2019). The reactivation of tuberculosis may be associated with poor nutrition in patients who have had a gastrectomy. Research findings suggest that individuals with malnourishment have an exceptionally elevated risk of tuberculosis infection (Sundre *et al.,* 1992). Cattle rearing (P = 0.026, OR = 4.028) and a history of tuberculosis (OR = 1.362) were the other significant risk factors of *Mycobacterium tuberculosis* infection observed in our study.

Conclusion

Among the 100 patients who were recruited for this study, the overall prevalence of pulmonary tuberculosis was 23.0%. Of the *Mycobacterium tuberculosis* cases found, 8.7% had TB that was resistant to rifampicin. Our study found a significant age-based distribution of *Mycobacterium tuberculosis* infection (P = 0.020). The distribution of the infection varied statistically significantly (P = 0.003) according to the patients' marital status. Nonetheless, compared to patients who were single, married patients had a higher risk of the infection (OR = 4.141). Those who lived in rural areas had a higher infection risk (OR = 1.273). Our study revealed that malnutrition, cattle rearing, and a history of tuberculosis were significant risk factors for pulmonary tuberculosis. Health facilities should use the GeneXpert assay to quickly diagnose tuberculosis and identify cases of multi-drug resistant TB. This will enable a more efficient and timely course of treatment.

Conflict Of Interest
The authors declare no conflict of interest in this study.

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