Original Research Article

A Retrospective Analysis of *Mycobacterium tuberculosis* in a Tertiary Healthcare Facility in Jos, North Central Nigeria.

ABSTRACT

Background: Tuberculosis remains a major health problem in developing countries. The GeneXpert Mycobacterium tuberculosis and rifampicin resistance (MTB/RIF) assay is a new test in in many communities in Nigeria that is revolutionizing *Mycobacterium tuberculosis* control by contributing to the rapid diagnosis of tuberculosis and rifampicin resistance.

Aim: This study aimed to determine the prevalence of *Mycobacterium tuberculosis* and rifampicin-resistantat North-Central Tuberculosis Reference Laboratory (NCTBRL) in Jos, North-Central Nigeria.

Study Design: Retrospective examination of hospital records.

Place and Duration of Study: North-Central Tuberculosis Research Laboratory (NCTBRL) Jos, North-Central Nigeria between January and December 2019.

Methodology: This was a retrospective study of archival records of 2719 patients screened for *Mycobacterium tuberculosis* and rifampicin-resistant using GeneXpert MTB/RIF assay. The samples comprised of sputum, ascitic fluid, gastric lavage, pleural fluid, abscesses, cerebrospinal fluid, urine, pericardial fluid and synovial fluid,from patients with suspected pulmonary tuberculosis (PTB) or Extrapulmonary tuberculosis (EPTB).The results obtained were analyzed using SPSS version 26.0 (SPSS Inc., Chicago, IL, USA) statistical software.

Results: Overall, 212(7.8%) of the total samples received were positive for *Mycobacterium tuberculosis*, with pulmonary tuberculosis (PTB) accounting for the majority of the cases. Male patients accounted for 59.9% of the cases compared to 40.1% in females. The infection was more among the age group 15-47 years and less common among the 0-14 age group. Rifampicin resistant MTB was detected in 2.3% of the cases, while 90.6% and 7.1% were sensitive and indeterminate to rifampicin respectively.

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Conclusion: The prevalence of Mycobacterium tuberculosis (MTB) was 7.8% with rifampicin-resistant of 2.3%. Appropriate diagnosis, treatment, and effectivesurveillance of MTB infections could reduce the incidences of rifampicin-resistant tuberculosis among the study population.

Keywords: Extrapulmonary tuberculosis, GeneXpert MTB/RIF assay, *Mycobacterium tuberculosis,* Pulmonary tuberculosis.

1. INTRODUCTION

Mycobacterium tuberculosis (MTB) is an aetiological agent of human tuberculosis identified by Robert Koch over a century ago. It is one of the ancient and deadliest neglected tropical diseases of mankind. Despite the effort at combating this disease, it still poses major health, social, and economic burdens primarily in low- and middle-income countries and in people living with HIV/AIDS[1] . It is a chronic necrotizing infection characterized by the presence of granulomatous lesions. The bacterium is a member of the *Mycobacterium tuberculosis* complex (MTBC), which includes: *Mycobacterium tuberculosis* (MTB), *M. africanum*, which causes tuberculosis (TB) in humans only in certain regions of Africa; *M. bovis*, *M. caprae,* and *M. pinnipedii*, causing TB in wild and domesticated mammals; *M. microti*, that causes TB only in voles [2]. Mycobacterium tuberculosis is known to cause both pulmonary tuberculosis (PTB) and extrapulmonary tuberculosis (EPTB) in men such as TB lymphadenitis, miliary TB, TB meningitis, cutaneous TB, pleural TB, ocular TB, Pott disease, and gastrointestinal TB [3]. Of all the possible types of tuberculosis, the most common is PTB, which has great epidemiological significance due to its extremely contagious nature. The proportion of patients with EPTB relative to those with PTB varies among countries and depends on associated diseases, risk factors, and ethnicity, with increasing frequency among patients with advanced immunosuppression [4].

Mycobacterium tuberculosis is a slow-growing organism with a doubling time of 12–24 hours under optimal conditions. A major feature of MTB is the peculiar cell wall structure, which provides an exceptionally strong impermeable barrier to noxious compounds and drugs, and that plays a fundamental role in virulence [5]. In 2019, TB remained the most common cause of death from a single infectious agent. Globally, an estimated 10.0 million people developed tuberculosis with approximately 1.2 million TB-related death among HIV-negative people and an additional 208,000 deaths among people living with HIV/AIDS. Most of these cases were in the WHO regions of South-

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East Asia and Africa with Nigeria accounting for 4.4% incidence [6]. Additionally, around 25% (2.7 billion people) of the world population has latent tuberculosis infection and is thus at risk of developing tuberculosis. Typical symptoms of active TB are chronic cough, hemoptysis, fever, night sweat, and often called consumption due to the associated significant weight loss, dramatically pale skin, ethereal thinness, with red cheeks and a feverish glow [7].

The diagnosis of TB is relatively simple and inexpensive, and in most cases can be cured with well-tolerated, effective, and low-cost treatments[8]. It has been estimated that 37 million patients were cured between 2000 and 2013, which was ascribed to advanced diagnostic methods in conjunction with effective treatments. However, multidrug-resistant tuberculosis (MDR-TB) remains a major challenge to achieving complete disease control. The outbreak of COVID-19 has also disrupted TB diagnosis and management as many developing countries have been reported to be using GeneXpert machines for COVID-19 causing further shortages of the already meagre TB diagnostic and treatment resources[9].

2. MATERIALS AND METHOD

This was carried out at the North-Central Tuberculosis Research Laboratory (NCTBRL) in Jos, North-Central Nigeria. The research laboratory is located in Jos, Plateau State of the North-Central region of Nigeria, and serves as a referral centre to all the neighbouring states. All specimens that were submitted to the NCTBRL were analyzed using the GeneXpert MTB/RIF machine according to the manufacturer's protocol: The Sample reagent was added in a 2:1 ratio in a 15 ml falcon tube, and the tube was manually agitated twice during a 15-minute incubation period at room temperature. Then, 2 ml of the inactivated material was transferred to the test cartridge with a sterile disposable pipette (provided with the kits). The cartridges were loaded into the GeneXpert machine. The entire laboratory procedure was performed using biosafety measures according to the standard laboratory protocol. The interpretation of data from the MTB/RIF tests was software-based and not user-dependent[10].

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3. DATA ANALYSIS

The results obtained were analyzed using Statistical Package for Social Sciences (SPSS) version 26 (IBM SPSS Inc, Chicago, IL, USA).

4. RESULTS

A total of 2719 samples were analyzed of which 2615 were sputum for suspected PTB, while 104 samples were different body fluids from suspected EPTB patients. The overall prevalence of MTB among the study population was 7.8%. Pulmonary tuberculosis was found to be the commonest with a prevalence of 8.0% compared to 3.8% for EPTB. The difference in the prevalence of PTB and EPTB among the study population was not statistically significant (P = 0.13) (Table 1).

This study revealed a significant relationship between MTB and sex. Out of 1339 male patients that were tested, 127(9.5%) were positive for MTB compared to 85(6.2%) positive female patients. This difference was statistically significant at P = 0.001 (Table 2).

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There was a statistically significant association between MTB infections and age groups (P < 0.001) (Table 3). A higher infection rate was observed among patients aged 15-47 years old as 1617 were screened, with 154(9.5%) positive. Age group ≥64 years accounted for 21(6.8%) infection rates out of 311 patients tested within this age group. This was followed closely by the group 48-63 years with a prevalence of 28(5.3%). The least prevalence rate of infection was observed among patients aged 0-14 years with a prevalence of 6(2.6%).

Out of the 212 positive samples for MTB, 5(2.3%) demonstrated resistance to rifampicin while 192(90.6%) and 15(7.1%) were sensitive and indeterminate respectively. Female patients accounted for 4(80.0%) of the resistant compared to 1(20.0%) in males. The distribution of rifampicin-resistant MTB according to sex was not statistically significant (P = 0.15) (Table 4).

Table 1: Prevalence of *Mycobacterium Tuberculosis* among the study population

MTB	Positive (%)	Negative (%)	Total
PTB	208(8.0)	2407(92.0)	2615
EPTB	4(3.8)	100(96.2)	104
Total	**212(7.8)**	**2507(92.2)**	**2719**

X^2 = 2.348

P = 0.13

d = 1

Table 2: *Mycobacterium Tuberculosis* in relation to sex

MTB	Sex Male (%)	Female (%)	Total (%)
Positive	127(9.5)	85(6.2)	212(7.8)
Negative	1212(90.5)	1286(93.8)	2498(92.2)
Total	**1339(49.4)**	**1371(50.6)**	**2710(100)**

$X^2 = 10.137$

P = 0.001

df = 1

Table 3: Distribution of *Mycobacterium tuberculosis* in relation to age group

Age	*Mycobacterium tuberculosis* Positive	Negative	Total
0-14	6(2.6)	228(97.4)	234(8.7)
15-47	154(9.5)	1463(90.5)	1617(60.2)
48-63	28(5.3)	496(94.7)	524(19.5)
≥64	21(6.8)	290(93.2)	311(11.6)
Total	**209(7.8)**	**2477(92.2)**	**2686(100)**

$X^2 = 20.517$

P < 0.001

df = 3

Table4: Prevalence of Rifampicin Resistant Tuberculosis Among the study population

Rifampicin	*Mycobacterium tuberculosis* Male (%)	Female (%)	Total (%)
Sensitive	118(61.5)	74(38.5)	192(90.6)
Indeterminate	8(53.3)	7(46.7)	15(7.1)
Resistant	1(20.0)	4(80.0)	5(2.3)
Total	**127(59.9)**	**85(40.1)**	**212(100.0)**

$X^2 = 3.778$

p = 0.151

df = 2

5. DISCUSSION

The Gene Xpert MTB/RIF assay has revolutionized the tuberculosis surveillance system as a useful tool in detecting and monitoring MDR-TB. The progress already made in TB monitoring in many countries of the world was disrupted in 2020 by the outbreak of COVID-19. The COVID-19 test is run on the same Gene Xpert machine meant for TB diagnosis and most countries reallocated the already limited machines to the test of COVID-19[11].The restriction of movements brought about by the pandemic also affected the treatment and surveillance of tuberculosis in most African countries.

The prevalence of MTB within the study period was found to be 7.8%, with PTB and EPTB accounting for 8.0% and 3.8% respectively. This was lower than the 11.9% reported in 2004 by Egah and his colleagues in a retrospective study conducted in Jos [12]. Similarly, a high prevalence of 22.0% was reported in Enugu state, South-east Nigeria, and 24.8% reported in a similar retrospective study in Calabar, Cross River State of South-south Nigeria [13,14]. This variation in reported prevalence even within the same country may reflect the variations in sample size, access to health care facilities, and effectiveness of TB control programs. Therefore, the low prevalence rate of MTB in this research could be due to increasing awareness and surveillance, improved housing and standard of living, accessible healthcare, and treatment of infected individuals as provided by the North-Central Tuberculosis Research Laboratory (NCTBRL).

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Since Nigeria was listed as one of the countries with a high burden of tuberculosis by WHO, the Nigeria National Tuberculosis Control Programme and its donor partners scale up community-based case finding, availability and accessibility to improved methods for TB diagnosis and effective treatment regimen which has resulted in reduced incidence of tuberculosis in the country[15].Despite these efforts at combating tuberculosis, the prevalence remains high in some parts of Nigeria mainly among patients living with HIV/AIDS. This assertion is supported by Corbett and his colleagues who revealed in their research that an increasing prevalence of HIV/IADS is responsible for increasing notification rates for TB[16]. In this research, there was no record of the HIV status of the patients for comparison.

It was observed that PTB was the most common among the study population. The reason for this may not be far fetch as MTB is mainly transmitted through aerosolized droplets with the primary focus of infection in the lungs. The majority of the samples received at the centre were sputum from suspected PTB cases with only a few for EPTB. Several studies have corroborated this finding that PTB is more common than EPTB. Risk factors such as being female, end-stage renal disease (ESRD), and HIV infections are given as some of the major risk factors for EPTB [17,18], while factors like smoking, diabetes mellitus, and use of immune-suppressive drugs/steroids were associated with PTB [19,20]. The probability of reactivation at an extra-pulmonary site after primary infection in the lungs may be higher in patients with confounding factors [21]. This study couldn't establish any confounding factor because such information was not found in the archival documents used for this research.

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This study showed that the prevalence of MTB is higher in males than females. This is in agreement with research conducted in Ethiopia which reported that men are significantly more at risk of contracting and dying from TB than women [22]. This is in contrast with studies conducted in some other countries that reported more prevalence in females[23,24]. Several reasons have been suggested to explain this gender variation in MTB prevalence. Less access to health care for women, and therefore more unreported MTB, has been mentioned as one of the factors contributing to low prevalence in females [25,26]. Another explanation for this is that most males engage in works and social interactions that can predispose them to TB infections than females.

This study revealed that the prevalence of MTB infections according to age group was statistically significant with age group 15-47 years reporting the highest prevalence rate. This age group is the most active workforce of any population and is also involved in activities that place them at high risk for TB. This finding is supported by the study of several studies that identified TB/HIV coinfection as responsible for the high rates in persons within this age group[27,28]. Knowing the age group at high risk is significant if targeted MTB preventive measures are to be employed as age is a crucial factor in shaping TB epidemiology. Symptoms, disease progression, and treatment outcomes of TB patients are known to vary with age, probably caused by changes in the immune response with age [29,30].

The prevalence of Rifampicin-resistant TB was 2.3% while 7.1% were indeterminate. This is lower than the report of studies from other parts of Nigeria and some African countries [31-33). The regional differences in the prevalence of drug-resistant TB could be as a result of variation in effective

surveillance systems and treatment of infected individuals. Inadequate therapeutic regimen, improper dosage, poor compliance with treatment regimens, and as well as the presence of comorbidities such as HIV/AIDS are some of the reasons for the high prevalence of MDR-TB in a population [34,35].

6. CONCLUSION

The prevalence of MTB infection and Rifampicin-resistant TB in this study is a thing of concern and require asustained and effective surveillance program to prevent its spread. There is need to create awareness among policymakers toencourage MTB screening among the general populace, and provide effective patient care.

LIMITATION OF THE STUDY

This study did not provide information on the outcome of treatment of the patients. There was no information on the presence of comorbidity such as HIV/AIDS or whether there was a case of relapse among the study population.

ETHICAL CONSIDERATION

The ethical clearance for this study was obtained from the Jos university Teaching Hospital Health Research Ethics Committee with reference number JUTH/DCS/IREC/127/XXXI/619.

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