Detection of Multi-drug Resistant *Mycobacterium tuberculosis* among Suspected Patients in Northeastern Nigeria

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Authors’ contributions

This work was carried out in collaboration between all authors. Author BAH designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors PFT and AFU participated in the design of the study and supervised the study. Authors MIM and BHJ managed the analyses of the study, wrote the final draft of the manuscript. Authors AMU, AA, AA and MTI managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

**Aim:** We determine the prevalence of TB and MDRTB within the study population. **Methodology:** The sampling consists of 192 (54.4%) males and 161 (45.6%) females. Zieheli Neelsen staining method was used for the detection of Acid Fast Bacilli (AFB) in the sputum samples collected. Rifampicin resistant (MDRTB) isolates were detected by GeneXpert and the conventional PCR technique.

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Results: In this study, 6 (9.5%) out of the 63 positive samples were rifampicin resistant Mycobacterium tuberculosis in which 4(6.3%) were found among females and 2 (3.2%) were found among males. Infection with Mycobacterium tuberculosis was not dependent on gender statistically in this study P=0.05. Secondary institution among the health care centers had highest cases of tuberculosis18 (33.3%) while tertiary institute had higher rifampicin resistant tuberculosis 5(2.5%). Statistically there was significant relationship between occurrence of tuberculosis and health care centers p<0.05. 

Conclusion: There is need to establish more reference laboratories within the country in order to address the rising cases of tuberculosis. There is also need for urgent attention of the government and other developmental partners to address the rising cases of MTB and MDRTB which is outside the expected ratio of 3:1 (male : female) stipulated by the World Health Organisation (WHO) and to conduct a national tuberculosis drug resistance survey so as to determine the actual burden of MDRTB in Nigeria.

Keywords: Multi drug-resistant tuberculosis; acid fast bacilli; rifampicin.

1. INTRODUCTION

Tuberculosis is a deadly chronic infectious disease which causes progressive body wasting, it was introduced into Africa by European traders, explorers and occupation forces and it decimated the African population alarmingly. Tuberculosis (TB) is an infectious disease caused by various species of mycobacteria, especially Mycobacterium tuberculosis and is a very important pathogen of humans which usually attacks the lung [1]. Tubercle bacilli spread in the host by direct extension, through the lymphatic channels and bloodstream, and via the bronchi and gastrointestinal tract [2].

Tuberculosis is a major public health problem in Nigeria, a country of 180-190 million inhabitants, with the country currently ranking 10th among the 22 high TB burden countries of the world and fourth highest in Africa (after South Africa, Ethiopia and Democratic Republic of Congo).

Multidrug-resistant M. tuberculosis (resistant to both isoniazid and rifampin) is a major and increasing problem in tuberculosis treatment and control. Such strains are prevalent in certain geographic areas [2]. Standard anti-TB drugs have been used for decades, and resistance to the medicines is growing. Disease strains that are resistant to a single anti-TB drug have been documented in every country surveyed (WHO, 2012).

Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs (Preskott et al. 2011). The primary cause of MDR-TB is inappropriate treatment. Inappropriate or incorrect use of anti-TB drugs, or use of poor quality medicines, can all cause drug resistance [3]. Disease caused by resistant bacteria fails to respond to conventional, first-line treatment. MDR-TB is treatable and curable by using second-line drugs. However second-line treatment options are limited and recommended medicines are not always available. The extensive chemotherapy required (up to two years of treatment) is more costly and can produce severe adverse drug reactions in patients. In some cases more severe drug resistance can develop.

About 450 000 people developed MDR-TB in the world in 2012. More than half of these cases were in India, China and the Russian Federation (WHO, 2012). The American embassy in Nigeria reported in 2010 an estimated number of MDR-TB cases among the notified 2,400 TB cases, out of which 21 cases were new and 23 cases were undergoing treatment (American embassy report, 2012).

The emergence of MDR-TB in the Nigeria also poses a threat, which if not effectively addressed, may wipe out the achievements of previous efforts in controlling TB. In view of this there is the need for evaluating the prevalence of MDR-TB in the Nigeria particularly in North-eastern part. In a case study conducted in infectious Diseases Hospital, Kano, out of 80 patients sampled, 52 were diagnosed to be Acid Fast Bacilli (AFB) positive and 28 were Acid Fast Bacilli negative. A 61.5% and 38.5% prevalence were found in male and female patients respectively, with age group 31-40 years having the highest prevalence of 28.8% [4]. Sputum smear microscopy remains the most common way to diagnose pulmonary TB. Depending on
the report and method used, sputum microscopy can accurately detect TB in 20% to 80% (using fluorescence microscopy methods) of TB cases [5]. The prevalence of MDR-TB is rising throughout the world more especially among those undergoing treatment or previously treated. MDR TB has lately become a major public health problem that threatens progress made in TB care and control worldwide [6]. In addition to that, there has been no systematic population-based National Drug Resistance Surveillance in Nigeria. However, from isolated and limited studies and anecdotal reports, it is known that the problem of MDR-TB is an emerging public health problem in Nigeria. Poor infection control practices in overcrowded settings (especially in Internally Displaced Person’s camps in Borno State) and the poor knowledge of physicians in terms of drug combinations used for the treatment of pulmonary tuberculosis (PTB) also contributes greatly to the emergence of MDR-TB [7].

The need for this study is to provide the current trends and rates of the TB and MDR TB in the northeast region in comparison to previous works done. This will provide possible suggestions on the existing TB control policies to aid curb out the predisposing factors due to insurgency in the northeast region especially Borno State and country at large.

It will also encourage for further studies on the MDR TB and XDR TB which poses threat to the whole nation and the world at large. This will lead to further researches and discoveries of new effective drugs against the MDR TB and XDR TB. Hence, this research aimed to investigate TB and MDR-TB among asymptomatic patients and their respective attending health care institutions within Borno State.

2. MATERIALS AND METHODS

2.1 Collection of Sputum Samples

Samples were collected from patients attending various health facilities (Internally Displaced Person Camp Clinics, Directly Observed Therapy Clinic, Primary Health Care Centers, other clinics within the State) which were referred to the University of Maiduguri Teaching Hospital tuberculosis reference laboratory center.

Patient was asked to rinse his or her mouth twice with water and inhaled deeply, coughed vigorously, and expectorated the sputum into sterile universal container (Cephied, 2012).

2.2 Sample Analysis

2.2.1 Microscopic examination of sputum for *Mycobacterium tuberculosis*

Slides were labelled appropriately and drops of sputum placed on the center using clean sticks and smeared. Smears were allowed to air-dry, fixed by passing through flame three times and covered with carbol fuchsin stain for 5 minutes. Decolorized with 3% v/v acid alcohol sufficiently and covered with methylene blue for 2 minutes and allowed to air-dry. Slides were examined microscopically using x100 oil immersion objectives (Cheesebrough, 2006).

2.2.2 Examination of sputum samples using gene Xpert

GeneXpert was used to diagnose TB and to test for rifampicin (RIF) resistance which was used as proxy for MDR-TB. Two ml of sample reagent (containing sodium hydroxide and isopropanol) was poured to 1 ml of the sputum samples (2:1 v/v). The mixtures were shook vigorously and incubated for 10 mins at room temperature. Samples were shook again and reincubated for an additional 5 mins. Sample mixtures were transferred into the sample chamber of the Xpert machine and test samples analysed. Results were displayed on the screen as Rifampicin Resistant Detected or Rifampicin Resistant Not Detected (Cephied, 2012).

2.2.3 Isolation and characterization of *Mycobacterium tuberculosis*

One millilitre each of sodium hydroxide and sodium citrate were added to 1 ml of the sputum, shook and allowed to stand for 15 mins at room tempature with occasional shaking. Centrifuged at 3000x g for 15 mins and the supernatants were poured. Fifteen ml of sterile saline added, centrifuged at 3000x g for 15 mins and the supernatant discarded. Centrifuged sediments were inoculated on to the Lowenstien Jensen slopes, cultures were incubated at 37°C for four weeks and observed on weekly basis. Colony morphology were read and taken in to consideration which include colour, texture, pigmentation, growth rate and Ziehl neelsen reaction. Characterisation of *Mycobacterium tuberculosis* was done using niacin, nitrate and catalase test [8].
2.3 Detection of Rifampicin (RIF) Resistant Gene Using PCR

2.3.1 Deoxyribonucleic acid (DNA) extraction

Using a wireloop a small portion of the solid colony was transferred in to labelled 2 ml centrifuge and DNA was extracted using manufacturer’s instruction (Hain Line Probe Assay, 2016).

2.3.2 Primer design

Oligonucleotide primer sequences used was as follows: The 2 oligonucleotide primers A1 and A2 resulting in the amplification of 180 -bp PCR fragments for detection of ropB gene (Rifampicin resistance gene); Primer A1: 5’- GCA TGT CGC GGA TGG AGC -3’. Primer A2: 5’- ACG CTC ACG TGA CAG ACC -3’ (Yang et al. 2011).

2.3.3 Polymerase chain reaction (PCR) amplification

AM-A (Amplication mix A) and AM-B (Amplication mix B) were removed from refrigerator and allowed to thaw out. Ten µl and 35 µl of the AM-A and AM-B were pipetted in to labelled 2 ml centrifuge tubes respectively and mixed gently by inverting 4 times. Forty five microliter of the master mix was pipetted in to the corresponding number of labelled 0.2 ml microcentrifuge tubes of the DNA samples and control (nuclease free grade water). Five microliter each of the sample DNA and negative control (nucleotide free grade water) were added to the tubes respectively. Followed by 35 µl primer nucleotide mixture, 5 µl of 10 x PCR buffer, 2 µl of MgCl₂, 3 µl nuclease free molecular grade water and 0.2 µl (1U) of HotStarTaq DNA polymerase. The amplification protocol consisted of 15 min of denaturation at 95°C, followed by 10 cycles comprising of denaturation at 95°C for 30 secs and 65°C for 20 mins. This was followed by 20 cycles compromising 95°C for 25 secs, 50°C for 40 secs and 70°C for 40 secs. Final extension was done at 70°C for 8 mins (Hain Line Probe Assay, 2016).

The amplified DNA was electrophoresed using 2% agarose gel, stained with ethidium bromide, and visualized under ultraviolet transillumination (Promega Company) and photographed.

2.4 Analysis and Interpretation of Results

The statistical analysis was done using SPSS Software version 16.0 and considered significant when p≤0.05. Chi-square was used to compare the variables at significance level of 0.05 (95% confidence interval).

3. RESULTS

In Table 1, the demographic distribution showed age group 16-30 years and 31-45 years had highest number of participants 99 (28.0%) and 147 (41.2%) respectively followed by age group 46-50 years 50 (14.1%). Least participating group were 76-90 years 7 (2.0%). Majority of the participants were civil servants 83 (23.5%), non-employed 70 (19.8%) and businessmen/traders 68 (19.3%). Least participating category was the retiree 26 (6.2%). Forty eight (13.6%) and 35 (9.9%) were males and females respectively. A total of 68 (19.3%) were businessmen/traders out of which 40 (11.3%) and 28 (8.2%) were males and females respectively while non-employed category had 23 (6.5%) males and 47 (13.3%) females.

Age group 31-45years with a total of 147(41.6%) had the highest number of participants, and out of which the positive tuberculosis cases was 27 (7.6%), followed by 16-30 years 24 (6.8%), 46-60years 8(2.3%), while the least was found within the age group of 61-75 years 4 (1.1%). No case was found among subjects within the age group of <15years and 76-90 years with 0 (0.00%) respectively as shown in Table 2.

The smear score showed that 34 (9.6%) had 10-99 tubercule bacilli in 100 fields (+) and 2 (0.6%) had 10 tubercule bacilli in at least 50 fields (++). Among female subjects, while 24 (6.8%) had 10-99 tubercule bacilli in 100 fields (+) and 3 (0.8%) had 10 tubercule bacilli in at least 50 fields (++). Among female subjects, Tubercule bacilli were not seen in 290 patients comprising of 156 (44.2%) male and 134 (38.0%) female subjects as shown in Table 3.

As seen in Table 4, the relationship between tuberculosis and occupation showed that businessmen/traders had the highest cases of tuberculosis 15 (23.8%) followed by farmers and non-employed subjects with 14 (22.2%) respectively, civil servants 9 (14.4%), students 6 (9.5%) and the least was found among retirees 5 (7.9%). Relationship between occupation and occurrence of tuberculosis was statistically significant (P<0.05).

GeneXpert results showed 2 (3.2%) rifampicin resistant and 34 (54.0%) non rifampicin resistant
Mycobacterium tuberculosis among the males while 4 (6.4%) rifampicin resistant and 23 (36.5%) non rifampicin resistant Mycobacterium tuberculosis among the female subjects (Table 5). A total of 290 negative for tuberculosis cases with 156 (53.8%) male and 134 (46.2%) female were detected. Relationship between gender and occurrence of rifampicin resistant/non rifampicin resistant Mycobacterium tuberculosis was statistically not significant (P>0.05) Table 5.

Table 1. Demographic distribution of the study subjects

| Ages   | Farmer | Bus./Traders | C. Servts | Students | N.employed | Retired | Total (%) |
|--------|--------|---------------|-----------|----------|------------|---------|-----------|
| 0-15   | 0      | 1             | 0         | 13       | 7          | 0       | 21(6.0)   |
| 16-30  | 6      | 12            | 6         | 43       | 32         | 0       | 99(28.0%) |
| 31-45  | 27     | 38            | 54        | 0        | 28         | 0       | 147(41.7%)|
| 46-50  | 11     | 14            | 23        | 0        | 2          | 0       | 50(14.1%) |
| 61-75  | 6      | 3             | 0         | 0        | 1          | 19      | 29(8.2%)  |
| 76-90  | 0      | 0             | 0         | 0        | 0          | 7       | 7(2.0%)   |
| Total  | 50     | 68            | 83        | 56       | 70         | 26      | 353(100%) |

Gender
- Male: 38, 40, 48, 29, 23, 14, 192(54.4%)
- Female: 12, 28, 35, 27, 47, 12, 161(45.6%)

Key: Bus./traders=Businessmen/trader, C servts=Civil servants N.emp. = Non-employed

Table 2. Distribution of tuberculosis based on age of subjects

| Age (Years) | Total (%) |
|-------------|-----------|
| <15         | 21(5.9)   |
| 16-30       | 76(21.5)  |
| 31-45       | 120(34.0) |
| 46-60       | 51(14.4)  |
| 61-75       | 19(5.4)   |
| 76-90       | 3(0.8)    |

Table 3. Intensity of Mycobacterium tuberculosis in relation to gender

| Gender | Mycobacterium tuberculosis smear result (%) | Total (%) |
|--------|--------------------------------------------|-----------|
|        | Negative | One plus(+) | Two plus(++) |        |
| Male   | 156(44.2) | 34(9.6)     | 2(0.6)       | 192(54.4) |
| Female | 134(38.0) | 24(6.8)     | 3(0.8)       | 161(45.6) |
| Total  | 290(82.2) | 58(16.4)    | 5(1.4)       | 353(100)  |

Key:
- 0 Tubercule bacilli in 100 fields (Mycobacterium tuberculosis negative)
- 1-9 Tubercule bacilli in 100 fields Actual Number Reported
- 10-99 Tubercule bacilli in 100 fields (+)
- 10 Tubercule bacilli /fields in at least 50 fields (++)
- >10 Tubercule bacilli /field in at least 20 fields (+++)

Table 4. Distribution of tuberculosis in relation to occupation of subjects

| Occupation | Prevalence of tuberculosis (%) | Total (%) |
|------------|--------------------------------|-----------|
|            | Positive | Negative |        |
| Farmers    | 14(22.2) | 36(12.4) | 50(14.2) |
| Business/Trader | 15(23.8) | 53(18.3) | 68(19.3) |
| Civil Servants | 9(14.4) | 74(25.5) | 83(23.5) |
| Student    | 6(9.5)   | 50(17.2) | 56(15.9) |
| Non Employed | 14(22.2) | 56(19.3) | 70(19.8) |
| Retired    | 5(7.9)   | 21(7.2)  | 26(7.3)  |
| Total      | 63(100)  | 353(100) |          |

$X^2$ calculated value = 0.041; df = 5; P<0.05= $H_0$ Accepted
Table 5. Rifampicin resistant and non rifampicin resistant tuberculosis in relation to gender of subjects

| Gender | Rif. resist. and Non-Rif. resist tuberculosis (%) | Total (%) |
|--------|---------------------------------------------------|-----------|
|        | Rif resist TB | Non- rif resist TB |          |
| Male   | 2(3.2)       | 34(54.0)        | 192(54.4) |
| Female | 4(6.4)       | 23(36.5)        | 161(45.6) |
| Total  | 6(9.5)       | 57(90.5)        | 353(100)  |

$X^2$ calculated value = 0.417 df = 2 $P > 0.05 = H_0$ Accepted

Key: Rif. Resist. TB = Rifampicin Resistant Tuberculosis. Non-Rif. Resist.TB = Non-Rifampicin Resistant Tuberculosis

The age group 16-29 years had the highest number of rifampicin resistant tuberculosis 3 (4.8%) and 21 (33.3%) non rifampicin resistant tuberculosis which is followed by the age group 46-60 years 2(3.2%) rifampicin resistant and 6 (9.5%) non rifampicin resistant. One (1.6%) MDRTB and 26(41.3%) non-MDRTB were seen among the age group 30-45years. The age group less than 15 years and 76-90years had 0 (0.0%) cases of both non-MDRTB and MDRTB respectively. Relationship between MDRTB and non-MDRTB and age groups was statistically not significant ($P>0.05$) as shown in Table 6.

Businessmen/traders had the highest cases of rifampicin resistant 3 (4.8%), followed by non-employed 2 (3.2%) and farmers 1 (1.6%). Non rifampicin resistant tuberculosis cases was highest among farmers 13 (20.6%) followed by non-employed and businessmen/traders with each 12 (19.0%). There was no rifampicin resistant Mycobacterium tuberculosis 0(0.0%) among the civil servants with 9 (14.3%) non-rifampicin resistant Mycobacterium tuberculosis. No rifampicin resistant Mycobacterium tuberculosis was detected among Students 0 (0.0%) with 6 (1.6%) non-rifampicin resistant Mycobacterium tuberculosis cases. Retirees were the least participating group with 0 (0.0%) rifampicin resistant Mycobacterium tuberculosis and 5 (7.9%) non-rifampicin resistant Mycobacterium tuberculosis cases. Relationship between occupation and occurrence of rifampicin resistant Mycobacterium tuberculosis was statistically significant ($P≤0.05$) as shown in Table 7.

As shown in Table 8, Tertiary health institutions had the highest number of rifampicin resistant 5 (2.5%) with 28 (14.2%) non rifampicin resistant tuberculosis cases while primary health center with 1(1.1%) rifampicin resistant case and 11 (11.0%) non rifampicin resistant tuberculosis cases. Secondary health institution had the highest number of non-rifampicin resistant tuberculosis with 18 (33.3%) with 0 (0.0%) case of rifampicin resistant Mycobacterium tuberculosis while tertiary institution has the least cases 28 (14.2%) of non rifampicin resistant tuberculosis. Relationship between health care institutions and occurrence of tuberculosis was statistically significant ($P<0.05$).

The migration of amplified Deoxyribonucleic Acid (DNA) segment of rifampicin resistant Mycobacterium tuberculosis on 2% agarose gel, Molecular marker marked M, positive bands 1-6 (rpoB gene) and a negative control 7. The molecular marker has 10 points of migration, each point representing 100 base pairs (bp) of the genome. The migration of the rpoB genes were at 180 bp as shown Fig. 1.

Table 6. Distribution rifampicin resistant tuberculosis and non-rifampicin resistant tuberculosis in relation to age

| Tuberculosis Status | Age (Years) | Total (%) |
|---------------------|------------|-----------|
| Rif. Resist. TB     | <15        | 2(3.2)    | 6 (9.5)   |
|                     | 16-29      | 3(4.8)    |           |
|                     | 30-45      | 1(1.6)    |           |
|                     | 46-60      | 2(3.2)    |           |
|                     | 61-75      | 0(0.0)    |           |
|                     | 76-90      | 0(0.0)    |           |
| Non-Rif. Resist. TB | <15        | 0(0.0)    |           |
|                     | 16-29      | 21(33.3)  |           |
|                     | 30-45      | 26(41.3)  |           |
|                     | 46-60      | 6(9.5)    |           |
|                     | 61-75      | 4(6.3)    |           |
|                     | 76-90      | 0(0.0)    |           |
| Total               | <15        | 2(3.2)    | 6 (9.5)   |
|                     | 16-29      | 24(38.1)  |           |
|                     | 30-45      | 27(42.9)  |           |
|                     | 46-60      | 8(12.7)   |           |
|                     | 61-75      | 4(6.3)    |           |
|                     | 76-90      | 0(0.0)    |           |
|                     |            | 63(100)   |           |

$X^2$ calculated value = 0.279 df = 10 $P>0.05 = H_0$ Accepted

Key: Rif. Resist. TB = Rifampicin Resistant Tuberculosis. Non-Rif. Resist.TB = Non-Rifampicin Resistant Tuberculosis
Table 7. Cases of rifampicin resistant tuberculosis (MDRTB) based on occupation

| Occupation       | Mycobacterium tuberculosis (%) | Total (%) |
|------------------|-------------------------------|-----------|
|                  | Rifampicin resistant | Non rifampicin resistant |          |
| Farmer           | 1(1.6)                      | 13(20.6)  | 14(22.2) |
| Business/Traders | 3(4.8)                      | 12(19.0)  | 15(23.8) |
| Civil servants   | 0(0.0)                      | 9(14.3)   | 9(14.3)  |
| Students         | 0(0.0)                      | 6(9.6)    | 6(9.6)   |
| Non-employed     | 2(3.2)                      | 12(19.0)  | 14(22.2) |
| Retired          | 0(0.0)                      | 5(7.9)    | 5(7.9)   |
| Total (%)        | 6(9.6)                      | 57(90.4)  | 63(100)  |

$\chi^2$ calculated value = 0.022; df =10; $P<0.05$; $H_a$ = Accepted

Table 8. Number of rifampicin/ non-rifampicin resistant tuberculosis (%) within health care centers

| Health care centers         | Non rifampicin resistant/rifampicin resistant tuberculosis (%) | Total (%) |
|-----------------------------|---------------------------------------------------------------|-----------|
|                             | Rif. resistant | Non Rif. resistant | Negative |
| Primary Health Center       | 1(1.0)         | 11(11.0)          | 90(87.9)  | 102(100) |
| Secondary Health Institution| 0(0.0)         | 18(33.3)          | 36(66.7)  | 54(100)  |
| Tertiary Health Institution | 5(2.5)         | 28(14.2)          | 164(83.3) | 197(100) |
| Total (%)                   | 290(100)       | 57(100)           | 6(100)    | 353(100) |

$\chi^2$ calculated value = 0.041; df = $P<0.05$; $H_a$ Accepted

Fig. 1. Electrophoresed photo of rifampicin resistant *Mycobacterium tuberculosis* gene (rpoB gene)

Key: M= Molecular marker, 1-6= rpoB gene positive isolates, 7= Negative control

4. DISCUSSION

Tuberculosis (TB) continues to occupy a prominent place among the major infectious diseases in underdeveloped and developing countries. The increase in tuberculosis cases has mostly been due to the emergence of AIDS in the 1980s, together with factors of impoverishment, social disorder, and lack of investment in effective disease control programs (Souza, 2006). This study was design to detect the multidrug resistant tuberculosis (rifampicin resistance) and cases of *M. tuberculosis* among patients attending and referred to the University of Maiduguri Teaching Hospital in Borno State, North east geopolitical zone of Nigeria.
Sixty three samples, (17.8%) had smear-positive TB in this study, this is in contrast to the 48 (34.4%) of Rasaki, et al. [9] and that of Egbe, et al., [10] in Nasarawa State which showed higher prevalence of 26.3%, but almost agrees with the findings of Lawson et al. [11] with 31 (18.2%). A higher prevalence was reported in Niger by Ibrahim, et al. [12] however, lower than 8% smear positivity was also reported by Boyer, et al. [13]. This could be attributed to the intense effort by the developmental organisation and Nigerian government towards providing timely diagnosis and treatment of tuberculosis within the State.

Highest prevalence was seen among age group 16-30 years 24 (6.8%). This is in contrast to the finding of Imam and Oyeyi, [14] in which the age group 30-43 years had the highest prevalence 145 (17.0%). Possibly due to active participation of such age group in daily life which lead to increase in chances of contracting and disseminating of tuberculosis.

There was male preponderance of tuberculosis (TB), 36 (57.2%) as compared to female 27 (42.9%); this was also in agreement with the studies of Rasaki, et al. [9] and also in concur with the work of Taura, et al. [4] where male subjects had prevalence of 61.5% as against 38.5% of females. There was no association between tuberculosis and gender statistically (P>0.05). This also agrees with World Health Organisation (WHO) report of higher TB rate among men than women [3]. Also Nyamogoba, et al. [15] reported a higher tuberculosis rate in males in Kenya. However, the findings in this study of a high rate of tuberculosis among women (42.9%), greater than the expected 3:1 ratio, only seem to highlight WHO concern of increasing TB burden in women. Generally, may be due to inability to complete the full course of treatment, lack of discipline and adherence to drugs instructions.

This research showed that the highest number of tuberculosis cases occurred among businessmen/traders with 23.8%, which agreed with the work of Gyar et al. [16] who had 43.1% but negated the finding of Egbe et al. [10] who had highest tuberculosis number among farmers 34.1%. Least cases were found among retirees 7.9%, students 9.5% and 14.7% civil servants. This closely agreed with the work of Gyar et al. [16] who had least among civil servants 21.7%. The relationship between occupation and TB is significant (P<0.05) statistically in this study. Possibly due to moving from one place to another in trading of goods hence exposing them to higher risk of contracting tuberculosis.

Rifampicin resistance of 9.5% found in this study is higher than the previous studies done in Nasarawa by Egbe, et al. [10] in which they had 6.6%, and also that of Jos and Lagos 7% conducted by Dinic, et al. [17] and also the work of Rasaki et al. [9] where they had 7.2% rifampicin resistant but is closer with the findings of Adekunle et al. [18] where 8.6% were resistant to rifampicin. A study conducted in North eastern part of Nigeria had 7.3% prevalence in which Borno state alone showed 35.4% (Tilako et al. 2013). A contrast was seen with findings of Lawson et al. [11] where 19% isolates were resistant to rifampicin. This is may be as a result of the insurgency that decimated the males mostly reducing the number of males within the State and inversely increases females’ population.

Rifampicin resistant tuberculosis (TB) prevalence among the female is 2 times higher than the males, females were found to have 6.4% while the males 3.2%. This negates the findings of Tilako et al. (2014) who had found male to have prevalence of 9.64% while females had 2.91%. This may be due to inability to complete the full course of treatment and adherence to drugs instructions.

The age bracket of 16-30 exhibit high tendency of 4.7% MDRTB as compared to the other age groups, which is in contrast to the findings of Tilako, et al. (2014) that showed high frequency of 9.25% MDR-TB among age bracket of 46-60, but agrees with the findings of Imam and Oyeyi, [14], where 15-29 age group had the highest percent distribution. This could be due to the actively coming in contact with different sets of people as such age group are the most productive hence exposes them more to tuberculosis within the age groups. In this work, cases of TB is not dependent upon the age of the study subjects P>0.05.

Secondary health institution had the highest cases of non rifampicin resistant tuberculosis (33.3%) with zero cases 0 (0.0%) of rifampicin resistant tuberculosis while the least cases of non rifampicin resistant tuberculosis was seen within primary health institution (11.0%). These findings agree with the work of Rasaki et al. [9] with highest cases of 50.0% at the secondary institution and the least cases of 21.4% at the
primary institution. Highest prevalence of rifampicin resistant tuberculosis was seen within tertiary institution 2.5% in this study. This may be due to referral from other health care institutions as a result of inadequate facilities hence increases the number TB within tertiary institute. There was a relationship between occurrence of TB and health care institutions (P<0.05) in this research.

5. CONCLUSION AND RECOMMENDATIONS

The prevalence of tuberculosis (TB) when compared with other researchers’ work mentioned, it was noticed that there was a reduction in cases of TB in the northern Nigeria. The efforts of the developmental organisations and the government were yielding positive results.

There was a serious concern with regards to high cases of tuberculosis within age groups of 16-30 years which were the most productive population as seen this research.

Even though there was a high case of TB among males than females, there was also an unexpected change in the ratio of TB occurrence within the sexes as stipulated by World Health Organisation (3 males : 1 females) which present challenge to the concerned authorities.

Businessmen/traders were also among the occupations that interacts with the population most frequently and high cases of TB within such category rises an issue that needs to be concerned with in this work.

Despite high prevalence of rifampicin resistant TB of 9.5% in this work, Tilako et al. 2014 had found a higher prevalence of 34.4% in Borno State. Measures put in place in tackling TB in the State seems to be relatively working.

Another worrisome noted area was the increase of rifampicin resistant TB among the females than males 2:1 ratio. This critical outcome of this research poses a threat to TB elimination goals set by the developmental organizations in Nigeria.

Judging by the trends of TB within the age groups, 16-30 years had highest cases of rifampicin resistant TB. Our youth stands a shakeable feature free of TB unless serious measures taken.

Higher case of rifampicin resistant TB was also observed in the tertiary health institution which was mostly equipped with better TB diagnostic facilities than other health institutions as seen by the number of subjects in this study.

In general, there were some progress in the treatment and diagnosis of TB within the study population but some unexpected trends of TB seen were a huge blow to the measures taken to tackle TB by the developmental organisation and government in this work.

There is a need to establish more National Reference Laboratories (NRL) in Nigeria for technical support, quality assurance and surveillance. Several factors might be responsible to the development of MDR-TB. These include patient factors such as poor adherence of patients to first line anti-TB drugs, inappropriate treatment regimen, dosage and duration for treatment and non-compliance to national guidelines of TB treatment protocol by clinicians. Since drug-resistance is a dynamic phenomenon, it is pertinent to monitor the trend of drug-resistance periodically among patients presenting with TB symptoms. Adequate enlightenment should be given to patients for proper drug compliance, because inadequate dosage intake or non compliance on the part of the patients and clinician as well should be encourage to abide with the National Tuberculosis Protocol (NTP) in other to reduce the TB surge.

Other molecular techniques should be included and made available in order to detect other drug resistance that are not due to rifampicin, this will significantly increase TB case diagnosis on time.

World Health Organisation has already put in place guidelines for the management of drug-resistant TB. However, a conference held in Johannesburg in 2006 – jointly organised by the South Africa Medical Research Council, Center for Disease Control, and WHO recommended seven steps needed to control MDR-TB. These are outlined as follows:

1. The need to develop emergency response plans for MDR-TB.
2. The need to implement infection control precautions in healthcare facilities.
3. The need to establish capacity for clinical and public health managers to respond to MDR-TB.
4. The need to intensify research and development of anti-TB drugs and rapid diagnostic tests for MDR-TB.

CONSENT

As per international standard or university standard, patient’s written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the ethics committee of the University of Maiduguri Teaching Hospital, Nigeria.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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