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Prevalence of Pulmonary and Rifampicin-resistant Tuberculosis Among Patients Attending Federal Medical Centre, Yenagoa, Bayelsa State, Nigeria

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Abstract: The prevalence of tuberculosis and Rifampicin-resistant tuberculosis (RMP-TB) among patients showing symptoms of tuberculosis that visited Federal Medical Centre, Yenagoa, Bayelsa state, Nigeria was determined from June 2015 to December 2015. A total of 456 patients comprising 218(47.8%) males and 238(52.2%) females were examined using their sputum and gastric lavage samples. GeneXpert System was used to determine the TB and RMF-TB. Results showed that out of the 456 patients, overall tuberculosis prevalence was 88(19.3%), males recorded 48(10.5%) while females had 40(8.8%). The highest tuberculosis prevalence was recorded amongst 21-30 years and 31-40 years age groups (5.5%). Out of the 456 patients, total prevalence for Rifampicin resistance was 11(2.4%). Of these, females and male prevalence was 6(1.3%) and 5(1.1%) respectively. There was no significant difference (P>0.05) in prevalence between age and gender. The treatment and follow-up of existing cases is a key to preventing the spread of multi drug-resistant tuberculosis.

Keywords: Bayelsa state; Health care; Tuberculosis; Rifampicin-resistant tuberculosis.

1. Introduction

Tuberculosis (TB) is a communicable disease that can be transmitted from one person to another through close contact with a patient. Typically, tuberculosis is caused by *Mycobacterium tuberculosis*, a bacteria agent [1]. Authors have variously reported that TB mostly affects the lungs and it's ranked as one of the major deadly communicable diseases in the world [2-4]. As such, it's among the 10 leading cause of death globally [4]. According to Okorie, *et al.* [1], TB is a major public health challenge with high mortality rate especially in developing nations. TB is spread via inhalation of droplet nuclei aerosolized [1, 5] through coughing, sneezing and spitting of an infected patient. TB has an incubation period is 2 - 6 weeks [1].

Global TB prevalence rate appears to be increasing. For instance, in 2012 about 8.6 million new TB cases leading to 1.3 million dead were reported by World Health Organization [6]. In 2013, about 9.0 million people developed TB and 1.5 million died from the disease (including 360 000 HIV-positive patients) [7]. According to WHO [4], 10.4 million contacted TB leading to 1.8 million death (comprising of 0.4 million among people with HIV) worldwide in 2015. Despite the pandemic nature of TB, about 49 million people have survived TB infection between 2000 to 2015 [4]. Generally, over 95% deaths resulting from TB infections occurs in low and middle-income nations. WHO [4] also reported that 87% of new TB global cases occurred in 30 high TB burden countries, and 6 nations viz: Nigeria, China, South Africa, India, Pakistan and Indonesia account for about 60% of total TB cases worldwide.

TB affects all groups of people including children, adolescent and adult irrespective of sex. About 1 million children contacted TB in 2015 and of these, 17% died excluding children with HIV infection [4]. In Nigeria specifically, 280,000 cases of TB were reported in 2011 with 68% incidence case which is an indication of prevalence rate of 280 per 100,000 population according to WHO global tuberculosis report of 2012 [8].

The control of TB has been affected by multi-drug resistant (MDR-TB) and extensively drug-resistant (XDR) [1, 5, 9] and to lesser extent by HIV/AIDS [1]. According to Affusim, *et al.* [10], the prevalence of TB has been decline before the discovery of HIV/AIDs. This suggests the role of HIV/AIDs in tuberculosis prevalence especially MDR-TB strains of the causative agent. According to Kohli, *et al.* [11], 480,000 new cases of MDR-TB occurred globally leading to about 190,000 deaths. MDR-TB is associated to resistance of some major potent drugs of TB such as isoniazid (INH) and rifampicin (RMP). According to Cox, *et al.* [12], MDR-TB is TB cases that are

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resistance to both isoniazid and rifampicin. The authors further reported that drug resistant tuberculosis (XDR-TB) cases have additional resistance to a fluoroquinolone and second-line injectable agent. Typically, INH and RMP have been used for the treatment of all cases of TB disease [13, 14].

WHO recommended the use of the rapid/fast test (diagnosis is made in about 2 hours) Xpert MTB/RIF® for TB diagnosis and it has expanded substantially since 2010 [4]. The system is typically used to detect TB and resistance to rifampicin simultaneously in about 2hours against 48 hours sputum smear microscopy and approximately two months for culture [1]. Cox, *et al.* [15], Iram, *et al.* [16] reported that Xpert MTB/RIF is approved software for determination of TB and rifampicin-resistance diagnosis. The basic assumption is that rapid drug susceptibility testing would reduce the delay to start of appropriate second line therapy.

Rifampicin resistance contributes about 98.5% of MDR-TB [17]. Typically, the prevalence of MDR-TB is on the increasing trend globally [18, 19]. The prevalence of MDR and XDR-TB have been determined in several regions of the World including Khayelitsha, South Africa [12], Mbarara, South Western Uganda [20], patients referred to Debre Markos Referral Hospital, Ethiopia [21], some regions in Nigeria such as Ogun state [22, 23], Abia state [1, 24], Edo state [25], Kaduna state [8], Niger state [26], Borno state [27], Plateau state [28] among others. But information about tuberculosis prevalence is scares in literature in Bayelsa state. Therefore, this study aimed at investigating the prevalence of tuberculosis and rifampicin resistant tuberculosis among patients showing symptoms of TB that visited Federal Medical Centre, Yenagoa, Bayelsa state, Nigeria

2. Materials and Methods

2.1. Study Area

The study was conducted at the Federal Medical Centre (FMC) Yenagoa, Bayelsa State. Bayelsa State is located within Latitude 4^0 15^1 North and Latitude 5^0 and 23^1 south [29]. It is also within longitude 5^0 22^1 West and 6^0 45^1 East. It is bounded by Delta state on the East, Rivers state in the West and south and Atlantic Ocean in the Southern most parts. Bayelsa state has eight local government area viz: Ekeremor, Brass, Nembe, Ogbia, Southern Ijaw, Sagbama, Kolokoma/Okpokoma, Yenagoa. According to the 2006 census figures, Bayelsa has a population of about 1.7 million people [29]. But the population has significantly increased over the last 7 years. The climatic condition of the area is characterized by 50 – 95% and 28 ± 6ºC relative humidity and temperature respectively.

2.2. Study Population (participants)

The study population is made up of two hundred and eighteen males (218) males and two hundred and thirty eight (238) females with symptoms of tuberculosis in clinics and wards in FMC Yenagoa. The age of the subjects was between 2yrs-78yrs.

2.3. Selection Criteria

Inclusion: The following signs were use as selection criteria; persistence cough for at least two (2) weeks, weight loss, night sweat, swelling at the neck, hand or armpit and fever with any of the above.

Exclusion: diabetic patients and individuals with known case of cardiovascular diseases etc.

2.4 Sample Collection

Sample collection was carried out at the clinics and wards. The sputum samples were collected at the spot with a wide mouth leak-proof container for adult, gastric lavage was collected by the pediatricians in children.

2.5. Laboratory Analysis

GeneXpert System that has modules thermal and optical system, cartridge self-contained disposable, computer system software barcode scanner and optional accessories like printer and UPS was used for the determination of tuberculosis in the subjects. The system was carried out based on manufacturers' instruction as previously described by Van, *et al.* [30].

2.6. Start-up the Gene Xpert instrument

Note: Before starting specimen processing, the Gene Xpert instrument was checked proper functioning and the modules availability.

The Gene Xpert Dx instrument and computer was switched on. The software was allowed to boot and open. When it fails to open, the Gene Xpert Dx shortcut icon on the desktop was clicked. The software was logged in using user name and password. The modules were confirmed available by checking the status.

a) Preparation of Sample

The working area was disinfected using 0.5% hypochloride. Then each Xpert MTB/RIF cartridge was labeled with the sample ID with a affixed label. The specimen was left in leak-proof sputum collection container. The lid of sputum collection container was unscrewed and added was Sample Reagent 2:1(v/v) to the sample and the lid again was closed. It was vigorously shaken 10-20 times and then incubated for 10 minutes at room temperature. The specimen was again vigorously shaken 10-20 times and then incubation again until no visible clumps of sputum.

b) Preparing the Cartridge

The liquefied sample was aspirated into the sterile transfer pipette until the meniscus is above the minimum mark (=2ml). Then, the sample was slowly transferred into the open port of the Xpert MTB/RIF cartridge. The cartridge lid was closed and the lid snaps firmly into place. The test was started within 30 minutes of adding the sample to the cartridge.

c) Start the Test on the Gene Xpert Instrument

In the Gene Xpert Dx System window, CREATE TEST button was clicked. Then the scan Cartridge Barcode dialog box appeared and the barcode on the Xpert MTB/RIF cartridge was scanned. After these, the Create Test window appeared. Then after, the software automatically fills the boxes for the following fields: Select Assay, Reagent Lot ID, Cartridge SN, and Expiration Date. In the Sample ID box, the sample ID was typed or scanned. The sample ID is associated with the test results and is shown in the View Results window and all the reports. The start Test was clicked. In the dialog box that appears, username and password was put in. The instrument module door with the blinking green light was opened and the cartridge was loaded. The door was closed. The test starts and the green light stops blinking. When the test is finished, the light is turned off. After some time, the system releases the door lock at the end of the run, then the module door was opened and the cartridge removed.

d) Reading, Recording and Reporting

i) Viewing Results on Gene Xpert Software (Basic User Setting)

In the Gene Xpert Dx System window, VIEW RESULTS on the menu bar was clicked on. The View Results window appears. When the software reports error, invalid or no result, the test was repeated using the already prepared specimen and a new cartridge. When there is repeated error, Invalid or no result, manual troubleshooting was done to exclude technical problems.

ii) Reporting of Results

The software reported MTB not detected or MTB detected. While the rifampicin resistance result indicates Rif resistance not detected or Rif resistance detected.

2.7. Statistical Analysis

The data was subjected to Chi square test and significance was determined at $\alpha = 0.05$.

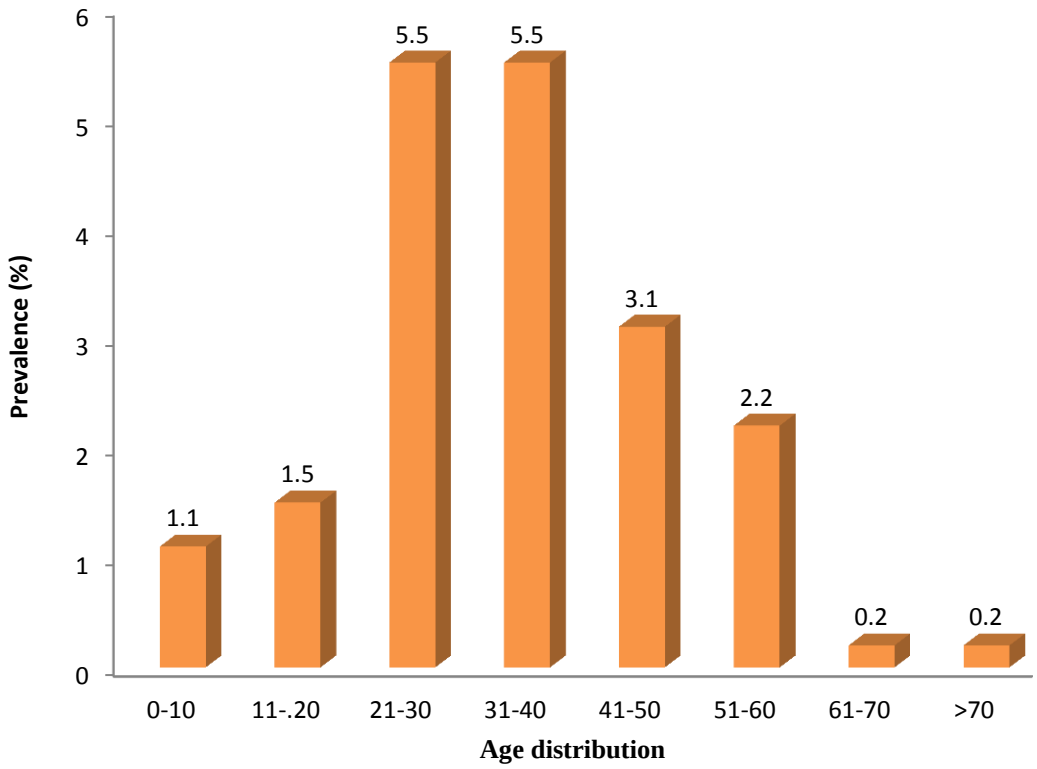
3. Results and Discussion

Figure 1 present the prevalence of PTB among patients that showed its symptoms attending clinics in Federal Medical Centre Yenagoa, Bayelsa state, Nigeria. A total of 456 patients was examined and 88 (19.3%) were positive for TB. Among the positive patient 5(1.1%), 7(1.5%), 25(5.5%), 25(5.5%), 14(3.1%), 10(2.2%), 1(0.2%) and 1(0.2%) were within the age group of <10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70 and 71 and above respectively. There was no significant difference (P>0.05).

Findings from this study revealed an overall PTB prevalence of 19.3% in Yenagoa, Bayelsa state. These findings had some similarity with reports from other parts of Nigeria including Abeokuta, Ogun state (19.7%) [22], Umuahia, Abia state (21.6%) [24], Edo state (15.7 %) [25], in patients attending National TB and Leprosy Training Center, Zaria and Barau Dikko Hospital, Kaduna City, Kaduna state (23%) [8], Benin city, Edo state (33.9%) [10], Minna and Suleja, Niger State (25.5%) [26], Maiduguri, Northern Nigeria (14.7%) [27]. But varies with the findings from prevalence among patient attending Nigerian Institute for Medical Research, Lagos and the Jos University Teaching Hospital, Jos (31.4%) [28] and some region in South- Eastern Nigeria (31.7%) [31].

The relatively lower prevalence recorded in this study (19.3%) compared to some region of Nigeria may be associated variation in geographical location and effectiveness in the directly observed treatment short-course strategy toward TB control. The variation in prevalence rate in this study compared to previous works could be due higher population level and prevailing activities of inhabitants in such region. Lifestyle, overcrowding environment and geographical/ climatic condition may increase the chance/ risk factor of contacting TB through aerosol from patients. Affusim, *et al.* [10] living conditions such less overcrowding and better nutrition, BCG vaccination and anti-TB chemotherapy are some of the conditions that reduces TB prevalence. According to Tomford [32], Okodua [22] high population and inhalation of aerosol droplets are major risk factors for TB.

Figure-1. Prevalence of PTB by Age among patient attending TB clinic in Federal Medical Centre, Yenagoa

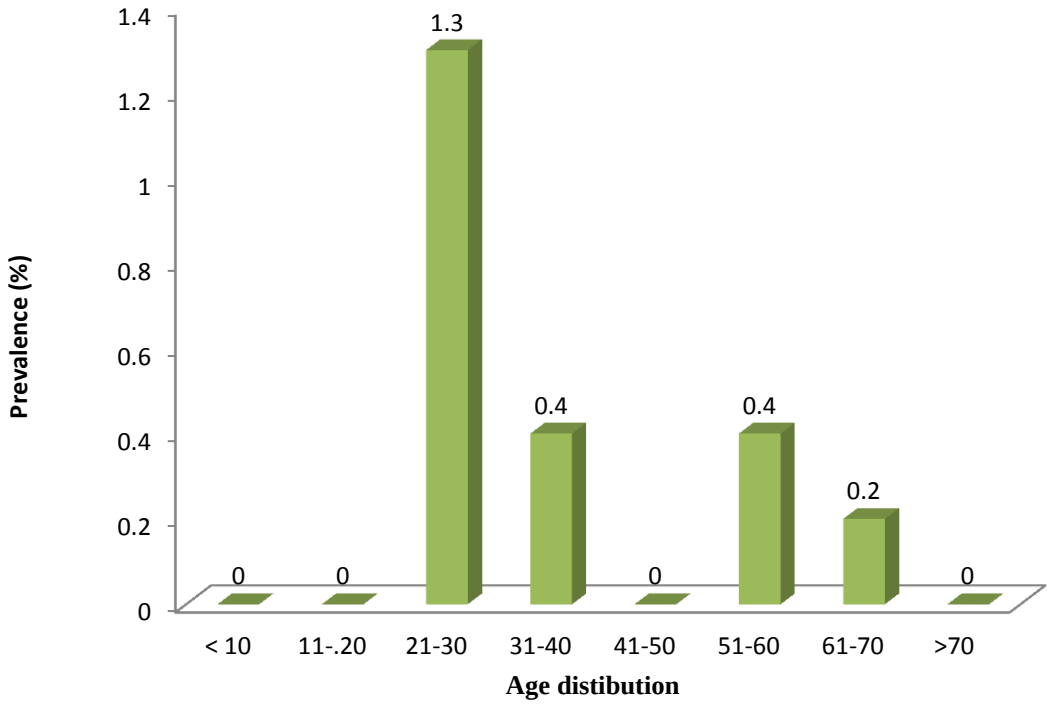


The prevalence of PTB among different age groups was highest (5.5%) in age group 21 – 30 and 31- 40 years. This finding is similar to 7.2% rate reported by Kamerbeek, *et al.* [33] among age group 25 – 35 years in Tygerberberg, South Africa. Itah and Udofia [31] reported that individuals within the age grade of 16 and 35 years are mostly affected by PTB in south eastern Nigeria. Sani, *et al.* [26] reported that patient between the age grade of 11-40 years are more susceptible to PTB in Minna and Suleja, Niger State. Nwobu, *et al.* [25] reported that PTB is usually higher among <20 years and 21– 30 years age grade in Benin, Edo state. Oluwaseun, *et al.* [34] reported prevalence of PTB as 17.3% and 8.8% in males and females in Abeokuta, Ogun state. Abiodun, *et al.* [23] reported prevalence of PTB of 37.3% and 62.7% for male and female respectively in Ikenne local government area of Ogun state. Accordingly, TB has its highest burden among young adults [35]. These reflected in the result of this study (Figure 1).

In this study, the prevalence of RMPR-TB patients with symptoms of TB among patients attending Federal Medical Centre Yenagoa, Bayelsa state, Nigeria is presented in Figure 2. Of 456 patients examined 11 (2.4%) was positive to MDR-TB. Among the various age group of 0-10, 11-20, 21-30, 31-40, 41-50, 51-60, 61-70 and 71 years and above, the positive patients prevalence were 0(0%), 0(0%), 6(1.3%), 2(0.4%), 0(0), 2(0.4%), 1(0.2%) and 0(0%) respectively. There is no significant variation (P>0.05) among the various age group. Poverty, ignorance and lack of quality health services could be a contributing factor of the prevalence rate determined in this study. The highest prevalence (1.3%) was seen in the age group of 21-30 years, which could be justified due to their active daily activities.

The prevalence of 2.4% in this study agrees with the global prevalence of 3.6% and 3.5% in 2010 and 2013 respectively as reported by WHO. But lower than the prevalence of 5.8% in Abeokuta, Ogun state [34] and 6.0% in China [36]. The variation in prevalence rate could be associated to several factors. For instance, Shamaei, *et al.* [37] reported that high MDR-TB rate could be due to spontaneous mutation of *M. tuberculosis* in the infected patients. In addition, infection with drug resistant strains of *M. tuberculosis* [18, 38] could also cause resistance. *M. tuberculosis* occur with other disease condition including HIV/AIDS [12], and some disease conditions caused by *Candida* species (such as *Candida albicans*, *tropicalis* and *C. glabrata* [39]. TB history of the participant/ subject could also determine the prevalence rate as well. According to Mulu, *et al.* [21], TB patients that had previous history of TB therapy is 2 times more likely to have *M. tuberculosis* infection than treatment of naïve patients. The authors further reported that TB patients who have used anti-TB drugs are 4.2 times more likely to develop rifampicin-resistant *M. tuberculosis* compared to treatment of naïve patients as well.

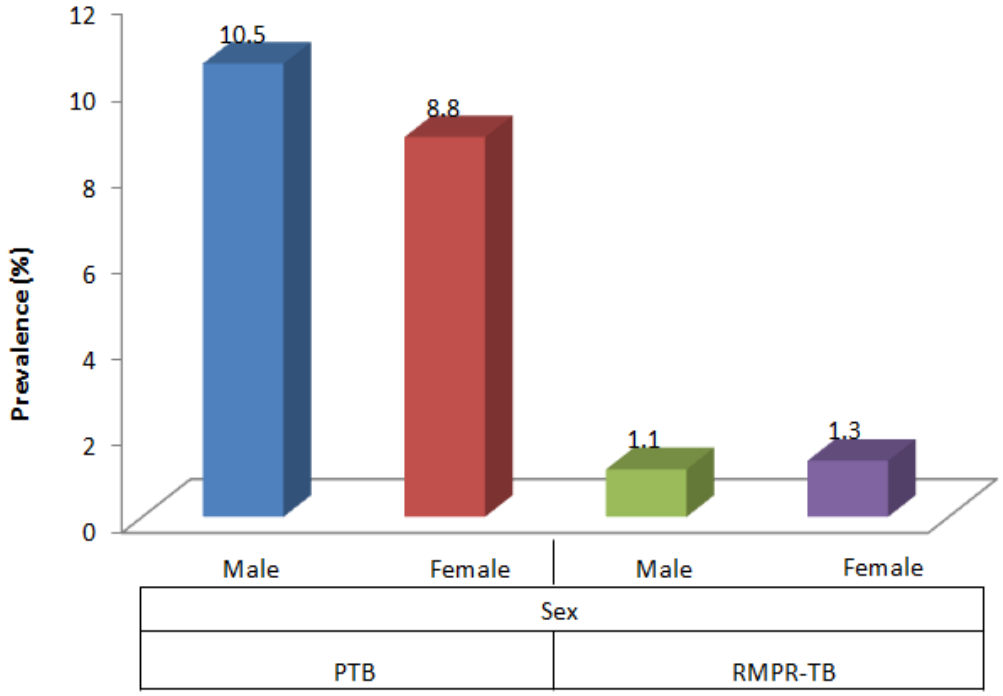
Figure-2. Prevalence of RMPR-TB by Age among patient attending TB clinic in Federal Medical Centre, Yenagoa



The prevalence of PTB and RMPR-TB of the 456 patients based on sex are presented in Figure 3. Of the 456 patients 218 were male and the rest 238 were female for PTB. Of this values, 48 (10.5%) and 40 (8.8%) was positive to PTB for male and females respectively, showing no significant variation (P>0.05) among the two sex category. Although, 5(1.1%) and 6(1.3%) male and female respectively was positive to RMPR-TB, being not significantly different (P>0.05). The distribution of PTB by the gender of the subjects showed a higher prevalence among males 10.8% compared to females (8.8%). This trend of observation has also been reported by various researchers. Borgdoff, *et al.* [40] reported female to male PTB prevalence ratio of < 0.5 in South-East Asia and West Pacific regions and approximately 1 in African continent.

According to Mulu, *et al.* [21], male is 2.17 times more likely to have *M. tuberculosis* infection compared to female. Other studies have showed the trend reported in this study. In Nigeria, prevalence of PTB among males and females were 35.5% and 26.9% respectively in South-Eastern Nigeria [31], 60.1% and 39.9% respectively in Minna and Suleja, Niger state [26]. Nwobu, *et al.* [25] reported PTB prevalence of 20.4% and 10.4% for male and females respectively in Edo state, Nigeria. Okodua [22] also reported that PTB prevalence is higher in males (18.1%) than in females (15.6%) in Abeokuta, Ogun state.

Figure-3. Prevalence of PTB and RMPR-TB disease cases by gender among patient attending TB clinic in Federal Medical Centre, Yenagoa



The higher prevalence of PTB among males could be as a result of frequent contact with infective droplets from diseased patients in vehicles, work place, etc. when they go out for daily activities [22]. The relatively higher RMPR-TB among females (1.3%) compare to males (1.1%) as observed in this study is comparable to the work of Shao, *et al.* [41] that reported MDR-TB prevalence of 19.0% and 15.8% in female and females among Chinese population. In Nigeria, Okodua [22] reported contrary prevalence of MDR-TB among males and females which was 19.7% and 14.3% respectively in Abeokuta, Ogun state. According to Okodua [22], the variation in the effect of gender in MDR-TB patients is multifactorial.

4. Conclusion

Tuberculosis (TB) remains a major global health problem. Multidrug-resistant tuberculosis (MDR-TB) caused by *M. tuberculosis* resistant to both INH and RMP with or without resistance to other drugs is among the most worrisome elements of the pandemic of antibiotic resistance. The study evaluated the prevalence of pulmonary tuberculosis and rifampicin-resistant tuberculosis among patient attending Federal Medical Center, Yenagoa, Bayelsa state, Nigeria. The study found that age group 21-30 years and 31-40 years had the highest prevalence rate. Based on RMPR-TB had apparently higher prevalence in female compare to male which was not significant. Based on the findings of this study we recommend that:

Rapid diagnostic assays to detect drug-resistant TB in other to prevent delays in treatment of MDR-TB and limiting its spread should be made available in health institutions.

Ethical Approval

The experimental protocol was approved by the Ethics Committee of the Federal Medical Centre, Yenagoa, Bayelsa state, Nigeria.

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