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RESEARCH PAPER

PULMONARY TUBERCULOSIS AND RESISTANCE PATTERN TO FIRST LINE ANTI-TUBERCULOSIS DRUGS IN A CITY OF WESTERN NIGERIA.

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ABSTRACT

This study determines the distribution of pulmonary tuberculosis (PTB) among suspected patients and the resistance pattern of *Mycobacterium tuberculosis* to first line anti-tuberculosis drugs. 609 suspected PTB subjects (based on chest x-ray), attending tuberculosis clinic at Sacred Heart Hospital, Abeokuta, were involved in this study. Their blood samples were screened for HIV antibody using WHO strategy II, while sputum samples were screened for the presence of acid fast bacilli (AFB) using standard method. All AFB positive samples were cultured and susceptibility tests done using 1% proportion methods. Results showed that of the 609 subjects, 19.7% had PTB. The observed infection, though not statistically significant, was higher among males (21.6%) than in females. However, significant differences were observed for PTB infections amongst various age groups. Susceptibility test revealed that resistance to streptomycin was highest (33.0%) compared to other drugs, while detected multidrug-resistant tuberculosis (MDR-TB) was 17.5%; being higher among males (19.7%) and in subjects with PTB only (19.3). In addition, mono-resistant and poly-resistance was found in 16.5% and 9.7% of the isolates respectively. These findings suggest that the control and prevention of PTB, especially MDR-TB, should include measures aimed at identifying the source of infection and proper treatment of infected individuals.

Key Words: Gender, Pulmonary tuberculosis, *Mycobacterium tuberculosis*, Susceptibility test.

INTRODUCTION

Tuberculosis is a global pandemic with 9.4 million incident cases in 2009 and 1.7 million deaths (WHO, 2009). It is ranked seventh amongst causes of global morbidity and mortality (Muray and Lopez, 1997). In 2010, Nigeria was ranked 4th among the 22 high tuberculosis burdened countries after India, China and South Africa (WHO, 2010a) and had nearly 460,000 cases in 2009 with 193,200 being sputum positive (WHO, 2010a).

Consequently, several anti-tuberculosis drugs have been developed. These drugs are usually classified as first-and second-line drugs (da Silva and Ainsa, 2007). The five first-line drugs include Isoniazid (INH), Rifampicin (RIF), Pyrazinamide (PZA), Ethambutol (ETB) and Streptomycin (SM) while those classified as second-line drugs include the Aminoglycosides (Kanamycin and Amikacin), the Polypeptide (Capreomycin, Para-aminosalicylic acid, Cycloserine), the Thionamides (Ethionamide, and Prothionamide), and Fluoroquinolones such as Moxifloxacin, Levofloxacin and Gatifloxacin.

The World Health Organisation (WHO) had recommended a standard regimen known as the Directly Observed Therapy, Short course (DOTS) (WHO, 1994), which consists of a 2 months initial phase of a daily dose of isoniazid, rifampicin, pyrazinamide (ATS, 1986) and ethambutol (Grange 1998) and followed by a 4 month-continuation-phase of isoniazid and rifampicin (ATS, 1986; Grange, 1998), given under direct observation (Schluger *et al.*, 1996).

The emergence of multidrug-resistant tuberculosis (MDR-TB), [Strains of *M. tuberculosis* that are resistant to both isoniazid (INH) and rifampicin (RIF) with or without resistance to other drugs] (Domingo, 2007) is worrisome because according to Dye *et al., (*2002), people with these strains, apart from transferring resistance strains to others, also fail treatment and thus, have a high risk of death. While resistance to either isoniazid or rifampicin may be treated with other first-line drugs, resistance to both isoniazid and rifampicin (MDR-TB) requires treatment with the second-line drugs such as Kanamycin, capreomycin, Para-aminosalicylic acid, cycloserine, ethionamide, levofloxacin and gatifloxacin (da Silva and Ainsa, 2007). These drugs have limited sterilizing effect and are not suitable for short course treatment (Sharma and Mohan, 2004).

Early detection of drug resistance strains of *M. tuberculosis* constitutes one of the priorities in the control of tuberculosis. It allows early initiation of the appropriate treatment of patients harbouring such resistance strains, and also in surveillance of drug resistance (Martin and Portaels, 2007). Detection of drug resistance in tuberculosis control programme can be carried out using phenotypic method and genotypic method (Martin and Portaels, 2007). The phenotypic method is mainly based on detection of growth of *M. tuberculosis* in the presence of antibiotic incorporated into appropriate media. The detection of such resistant strains can be carried out using the so-called "conventional methods". The genotypic methods detect the genetic determinant of resistance rather than the resistance phenotype. It involves two basic steps: nuclei acid amplification such as polymerase chain reaction (PCR), to amplify the sections of the *M. tuberculosis* genome that are altered in resistance strains; and a second step of assessing the amplified products for specific mutations correlating with drug resistance (Garcia de Viedma 2003; Palomino, 2005).

Since infection with MDR-TB means that such species of mycobacteria has lost its response to the main bactericidal drug –isoniazid, and the main sterilizing drug -rifampicin, the implication is that individuals infected with these stains remain infectious for a longer period, both in the hospital and the community. Also they require at least 12 months to possibly 24 months of treatment with less effective and more toxic second line drugs (Sharma and Mohan, 2004).

From the foregoing, data from countries like Nigeria are needed for proper and effective planning. This study therefore, intends to provide meaningful data on the distribution and resistance pattern of *M. tuberculosis* in Western Nigeria, as the availability of such data is limited in Nigeria.

MATERIALS AND METHODS

Study Area: This study was carried out in a Missionary Hospital in Abeokuta, a city in Western Nigeria. Abeokuta lies on latitude 7^{o}15N and longitude 3^{o}25E (Oyesiku and Kojeku, 1992). The city, which is about 81km South West of Ibadan and 106km North of Lagos, is located on an altitude of about 159m above sea level. It has a hot humid weather with annual rainfall of 963.3mm (Oyesiku and Kojeku, 1992). Its population is estimated to be 451,607 (National Bureau of Statistics, 2006). It has one Federal Medical Centre, few General Hospitals/Dental Clinics, several private hospitals/clinics and a Missionary Hospital (Sacred Heart Hospital), which apart from providing general health care delivery services, also serves as a referral centre for tuberculosis.

Sampling Method: Purposive sampling method as described by Araoye (2004) was used for selecting patients clinically suspected of having pulmonary tuberculosis (PTB) based on X-ray radiography. Patients who were on admission or those receiving treatment were excluded.

Sample size and duration: A total of six hundred and nine (609) subjects were finally selected for the study. The recruitment of samples lasted for two years (June, 2008 to May, 2010).

Sample Collection/Ethical Considerations: With informed consent, three sputum specimens were collected from each subject. These were 'first spot' specimen, an early morning specimen and a 'second spot' specimen (Horne, 1996). Two millilitres of blood samples were also collected from each subject.

Sample Analysis: The blood sample were screened for the presence of HIV antibody using the indirect solid phase enzyme immunoassay (EIA) method (immunocomb HIV-1 and HIV-2) as described by Orgenics. The screening was done according to manufacturer's instructions.

All the sputum specimens were processed in a safety cabinet for the presence of acid fast bacilli (AFB) and using Ziehl-Neelsen method as the staining technique (IUATLD, 1986). All the AFB positive sputum were cultured into

Lowenstein Jensen medium after decontamination with N-acetyl-L-cystein sodium hydroxide (NALC-NaOH) solution as described by Kent and Kubica (1985).

Preparation of drug solution and drug containing media: Isoniazid, rifampicin, streptomycin, ethambutol and pyrazinamide powders were obtained and were used to prepare bulk drug solutions with the following concentrations: Isoniazid (20µg/ml), rifampicin (4000µg/ml), ethambutol (200µg/ml), streptomycin (400µg/ml) and pyrazinamide (10000µg/ml) as described by Kent and Kubica (1985). The drug-containing Lowenstein Jensen medium was prepared by incorporating the various drugs into different Lowenstein Jensen medium before insipisation.

The required drug dosage was as described by Fujiki (2001). For isoniazid, 4 ml from the isoniazid solution was added to 400 ml of raw Lowenstein Jensen medium in a sterile flask to give 0.2 µg/ml. For rifampicin, 4 ml from the rifampicin solution was added to 400 ml of raw Lowenstein Jensen medium in a sterile flask to give 2 µg/ml. For ethambutol, 4 ml of the ethambutol solution was added to 400 ml of raw Lowenstein Jensen medium in a sterile flask to give 2 µg/ml. For streptomycin, 4 ml of the streptomycin solution was added to 400 ml of raw Lowenstein Jensen medium in a sterile flask to give 4 µg/ml. For pyrazinamide, 4ml of the pyrazinamide solution was added to 400ml of raw Lowenstein Jensen medium in a sterile flask to give 100 µg/ml.

The drug containing raw media were mixed properly and kept in the fridge overnight for proper diffusion of the drugs. Six millilitres [6ml] of the drug containing medium was later dispensed into sterile test tubes. The tubes were corked, labeled and inspissated at 90^{o}C for 50 minutes. Batches of drug free medium were also prepared for control.

Preparation of 1mg/ml Tubercle Bacilli Suspension: For each positive culture growth, about 5 drops of sterile distilled water were placed into a sterile screw capped test tube (homogenizer) containing about 5 – 6 sterile glass beads. Using a sterile wire loop, one loopful of *M. tuberculosis* complex growth was transferred into the homogenizer and was screw capped. This was vortexed for 3 minutes and left for 10 minutes to prevent aerosol from being produced. Five millilitres (5ml) of sterile distilled water was added and the large particles were allowed to settle. The supernatant suspension was transferred into another sterile test tube and was adjusted to that of MacFarland No 1 with sterile distilled water; this represents 1mg/ml bacillary suspension (Fujiki, 2001).

For the susceptibility testing, 0.01 mg/ml bacillary suspension (100% proportion) is usually used (Fujiki, 2001). The 0.01 mg/ml bacillary suspension was prepared by making a 1 in 100 dilution of the 1mg/ml bacillary suspension. This was achieved by adding 0.1ml of the 1mg/ml bacillary suspension to 9.9 ml of sterile distilled water. Another one in hundred (1/100) suspension was also made from the 0.01mg/ml bacillary suspension using sterile distilled water to produce 0.0001mg/ml (1% proportion)

For each 0.01mg/ml bacillary suspension, one drug-free (control) medium and a set of drug-containing media were inoculated with 0.1ml of the 0.01mg/ml suspension. Another drug-free control medium was inoculated with 0.0001mg/ml bacillary suspension (control of the 1% proportion).

The inoculum was allowed to spread on the surface of the medium and kept at slanting position with loosened caps at 37^{o}C in an incubator for one week and thereafter, the caps were tightened and incubation continued for 4 – 6 weeks. Immediately enough growth was observed on the drug-free control medium, the drug-containing tubes were brought out and read.

Interpretation of the susceptibility results: The growth on each of the drug containing medium was compared with the control tubes. No growth on the drug-containing medium or growth less than that of drug-free medium at 0.0001mg/ml dilution was recorded as sensitive (S) while growth on the drug-containing medium that was equal to or more than that on the drug-free medium at 0.0001mg/ml dilution was recorded as resistant (R).

Data analysis: Data were analyzed using the SPSS package. The student t test or the chi-square test was performed where applicable, to test for significant differences at $P < 0.05$.

RESULTS

Findings from this study revealed that of the 609 subjects examined, 315 were males while 294 were females. Sixty eight (68; 21.6%) of the males and fifty two (52; 17.7%) of the females had PTB. Though the PTB infection in males was higher than in females, the difference was not statistically significant (X^2=1.462; P=0.227) (Table 1).

Fifty seven (57; 18.1%) of the males and forty six (46; 15.6%) of the females had PTB only but the difference is not statistically significant (X^2=0.013; P=0.909) (Table 1). Eleven (11; 3.5%) of the males and six (6; 2.0%) of the females had PTB-HIV co-infection, but there was no significant difference in the infection rate (X^2=1.511; P=0.219). Twelve (12; 3.9%) of the males and twenty (20; 6.8%) of the females had HIV infection only; the difference was however not statistically significant (X^2=2.107; P=0.147) (Table 1).

The distribution of the total PTB in relation to age groups of the subjects revealed that, of the 28 subjects that were within the age range of 15-19 years old, 11 (39.3%) had PTB. Similarly, 169 of the studied subjects were of age range 20-29 years old, 194 were 30-39 years old, 153 were 40-49 years old, 37 were 50-59 years old and 28 were 60 years old and above. PTB infection rate among these age groups were 35 (20.7%), 34 (17.5%), 21 (13.7%) 8 (21.6%) and 11 (39.3%) respectively. There was significant difference in the total PTB infection rate in the various age groups (X^2=17.80; P=0.003) (Table 1). There was also significant difference in the total PTB infection rate among the various age groups of the female subjects (X^2=17.57; P=0.004) (Table 1).

TABLE 1: DISTRIBUTION OF PTB AND PTB-HIV CO-INFECTION AMONG THE STUDIED SUBJECTS BASED ON AGE AND SEX.

Age Range (Yrs)	Number tested			PTB ONLY			PTB-HIV			TOTAL PTB		
	M	F	T	M (%)	F (%)	T (%)	M (%)	F (%)	T (%)	M (%)	F (%)	T (%)
15-19	11	17	28	3 (27.3)	7 (41.2)	10 (35.7)	- (0)	1 (5.2)	1 (3.6)	3(27.3)	8(47.1)	11(39.3)
20-29	92	77	169	18(19.6)	13(16.9)	31 (18.3)	1(1.1)	3 (3.9)	4 (2.4)	19(20.7)	16(20.8)	35(20.7)
30-39	109	85	194	18(16.5)	10(11.8)	28 (14.4)	5(4.6)	1(1.2)	6(3.1)	23(21.1)	11(12.9)	34(17.5)
40-49	61	92	153	6 (9.8)	11 (12)	17 (11.1)	3(4.9)	1(1.1)	4(2.6)	9(14.8)	12(13.0)	21(13.7)
50-59	24	13	37	5 (20.8)	1 (7.7)	6 (16.2)	2(8.3)	- (0)	2(5.4)	7(29.2)	1(7.7)	8(21.6)
≥ 60	18	10	28	7 (38.9)	4 (40)	11 (39.3)	- (0)	- (0)	- (0)	7(38.9)	4(40.0)	11(39.3)
TOTAL	**315**	**294**	**609**	**57 (18.1) a**	**46 (15.6) a**	**103 (16.9)**	**11(3.5) b**	**6 (2.0) b**	**17(2.8)**	**68(21.6) C**	**52(17.7) C**	**120 (19.7)**
				χ^2 = 9.123 P = 0.104	**15.52 0.008**	**21.79 0.001**	**5.053 0.409**	**3.796 0.579**	**1.993 0.850**	**5.953 0.311**	**17.569 0.004**	**17.804 0.003**

KEY: M = Male; F= Female; T = Total; HIV= Human Immunodeficiency Virus, PTB= Pulmonary Tuberculosis; PTB-HIV= Pulmonary Tuberculosis and HIV co-infection

a $\Rightarrow$ χ^2 = 0.013 P = 0.909, b $\Rightarrow$ χ^2 = 1.511 P = 0.219, c $\Rightarrow$ χ^2 = 1.462 P = 0.227

Drug susceptibility pattern of the 103 isolates (61 from the male and 42 from the female patients) revealed that the resistant strains were generally higher among males compared to females, but the difference was not statistically significant (P>0.05) (Table 2). Likewise, MDR-TB in males 12 (19.7%) was also higher than that of females 6(14.3%) but the difference was not statistically significant.(X^2=0.500; P=0.480) (Table 2). Eleven of the 61 isolates in male and 6 of the 42 isolates in females were monoresistant but the difference was not statistically significant (X^2=0.253; P=0.619) (Table 2). Polyresistant is also higher in the isolates from males 8 (13.1%) when compared to those of females, 2 (4.8%) but the difference was not statistically significant (X^2=1.980; P=0.159) (Table 2).

Susceptibility results of the *M. tuberculosis* complex isolates also showed that, of the total 103 isolates (88 from PTB patients and 15 from PTB-HIV patients), multidrug resistant strains were recorded in one of the PTB-HIV

patient (6.7%) while 17 of the patients with PTB only had MDR-TB (19.3%) (Table 3). The sensitivity patterns recorded among the isolates from PTB patients and those from PTB-HIV patients showed no significant difference (P>0.05) (Table 3).

TABLE 2a: DISTRIBUTION OF THE DRUG SUSCEPTIBILITY PATTERNS OF *M. TUBERCULOSIS* COMPLEX BASED ON SEX OF THE SUBJECTS

					RIF(%)		INH (%)		ETB (%)		STR (%)		PZA (%)	
	NCS	**N MTB-C.I**	**MOT (%)**	**NC**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**	**S**	**R**
Sex														
M	68	61	0 (0)	7 (10.3)	44 (72.1)	17 (27.9)	41 (67.2)	20 (32.8)	55 (90.2)	6 (9.8)	37 (60.7)	24 (39.3)	53 (86.9)	8 (13.1)
F	52	42	4 (7.7)	6 (11.5)	35 (83.3)	7 (16.7)	32 (76.2)	10 (23.8)	39 (92.9)	3 (7.1)	32 (76.2)	10 (23.8)	38 (90.5)	4 (9.5)
T	**120**	**103**	**4 (3.3)**	**13 (10.8)**	**79 (76.7)**	**24 (23.3)**	**73 (70.9)**	**30 (29.1)**	**94 (91.3)**	**9 (8.7)**	**69 (67.0)**	**34 (33.0)**	**91 (88.3)**	**12 (11.7)**
					X^2= P=	1.747 0.186	X^2= P=	0.971 0.324	X^2= P=	0.226 0.635	X^2= P=	2.715 0.099	X^2= P=	0.312 0.576

Key: M= Male; F=Female; RIF= Rifampicin; INH= Isoniazid; ETB=Ethambutol; STR= Streptomycin; PZA=Pyrazinamide; MOT=Mycobacteria other than tuberculosis; MTB-C = *Mycobacterium tuberculosis* complex; NCS=number of cultured sputum; N MTB-C I= Number of MTB-C isolated, NC= Number Contaminated

TABLE 2b: DISTRIBUTION OF THE DRUG SUSCEPTIBILITY PATTERNS OF *M. TUBERCULOSIS* COMPLEX BASED ON SEX OF THE SUBJECTS.

					RIF (%)		INH (%)				
Sex	**NCS**	**NMTCI**	**MOT (%)**	**NC**	**S**	**R**	**S**	**R**	**MDR-TB (%)**	**Mono resistant**	**Poly resistant**
M	68	61	0(0)	7(10.3)	44 (72.1)	17 (27.9)	41 (67.2)	20 (32.8)	12 (19.7)	11(18.0)	8 (13.1)
F	52	42	4(7.7)	6 (11.5)	35 (83.3)	7 (16.7)	32 (76.2)	10 (23.8)	6 (14.3)	6 (11.5)	2 (4.8)
Total	**120**	**103**	**4(3.3)**	**13 (10.8)**	**79 (76.7)**	**24 (23.3)**	**73 (70.9)**	**30 (29.1)**	**18 (17.5)**	**17 16.5)**	**10 (9.7)**
					X^2= P=	1.747 0.186	X^2= P=	0.971 0.324	X^2=0.500 P=0.480	X^2=0.253 P=0.615	X^2=1.980 P=0.159

Key: RIF= Rifampicin; INH= Isoniazid; MDR-TB=Multidrug resistance tuberculosis; MOT=Mycobacteria other than tuberculosis; MTB-C = *Mycobacterium tuberculosis* complex; NCS=number of cultured sputum; N MTB-C I= Number of MTB-C isolated, NC= Number Contaminated

DISCUSSION

Findings from this study revealed an overall PTB prevalence of 19.7% in Abeokuta Nigeria with prevalence among new cases being 16.0%. These findings are in agreement with reports from other parts of Nigeria. For example, in Umuahia, Abia state, a prevalence of 21.6% was reported (Nwachukwu and Peter, 2010). Okodua *et al.* (2004) reported a prevalence of 21.7% in Edo State. In Maiduguri, Northern Nigeria, Ukwandu (1998) reported a

prevalence of 14.7% while Itah and Udofia (2005) reported a prevalence of 31.7% from South- Eastern Nigeria. In Lagos, a prevalence of 21.0% was reported by Idigbe and Onwujekwe (1983). The relatively lower prevalence recorded in this study (19.7%) compared to that in South-Eastern Nigeria (31.7%) could be as a result of the differences in geographical location and effectiveness in the directly observed treatment short-course (DOTS) strategy currently being used for tuberculosis control programme.

The highest prevalence reported for South- Eastern Nigeria (31.7%) could be due to higher population of inhabitants; as the main occupation in this region is trading which attracts more people from different locations. By this means, increasing the amount of infective droplets in the atmosphere and also increases the risk of being infected by TB. Higher inner city population and inhalation of infective droplets are risk factors for tuberculosis (Tomford, 2004). The higher PTB rate of 31.7% reported from South-Eastern Nigeria (Ita and Udofia, 2005) could also be due to the fact that the work was carried out during TB outbreak in the sub-region in March, 2001 (Ita and Udofia, 2005) and the work was carried out among patients on admission as well as out-patients. The present study was however carried out among out patients only.

The distribution of PTB by the gender of the subjects showed a higher prevalence among males 21.6% compared to females (17.7%). This trend of observation has also been reported by various researchers. In South-East Asia and West Pacific regions, female to male PTB prevalence ratio of less than 0.5 was reported (Borgdorff *et al.,* 2000). Itah and Udofia (2005) reported PTB prevalence of 35.5% among males and 26.9% among females in South-Eatern Nigeria. Idigbe and Onwujekwe (1983) had earlier reported PTB prevalence of 65% and 35% among males and females respectively in Lagos. 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. Tuberculosis is acquired through in inhalation of infectious droplets (Rose, 1991; Stead, 1992).

The relatively higher MDR-TB among males (19.7%) compare to females (14.3%) as observed in this study is in line with reports from South Africa where a higher number of MDR-TB cases was recorded in males (4826 cases) than in females (4615 cases) (WHO, 2010b). Similarly, in countries of the former Solviet Union such as Lithuania, male TB patients were found to harbour MDR-TB strains more than female (WHO, 2010b). The higher MDR-TB among males in this study is at variance with report from China where a higher MDR-TB was recorded among females (19.0%) than in male (15.8%) (Shao *et al.,* 2011). Reports from Australia, the Netherlands and United State of America showed that female TB patients harbor MDR-TB strains than male (WHO, 2010b). While males predominate among TB cases in most countries (WHO, 2010b), the variation in the effect of gender in harbouring MDR-TB is multifactorial. While the observation made from this study could be as a result of poor knowledge about TB as well as "male ego" that is common with males make them to seek alternative local herbs.

The relatively lower prevalence of MDR-TB recorded among isolates from PTB-HIV subjects (6.7%) compared with those from patients with PTB only (19.3%) ($P>0.05$) showed that occurrence of resistance was not related to HIV infection. This observation has been reported by Eyob *et al.* (2004) who reported 5.3% of MDR-TB among PTB-HIV patients in Ethiopia. This work is however at variance to that of Chakraborty *et al.,* (2010) who reported 17.7% and 6.6% MDR-TB in PTB-HIV patients and non HIV infected PTB patients respectively in India. The reason for this variation could be as a result of the high incidence of PTB in India which may have predisposed them to high incidence of MDR-TB. India is rated first among the 22 world high burdened TB countries (WHO, 2010b).
The surveillance of drug resistance in tuberculosis and most especially MDR-TB is a critical component of tuberculosis control. The benefits of this surveillance are numerous and these include increasing and strengthening of laboratory networks, improving on TB control programme and collection of adequate data.

While the laboratory services are fundamental in the control of tuberculosis, they are often the weakest component in the system. The importance of the laboratory in the control of tuberculosis should be recognized and the laboratory should be able to perform sputum smear microscopy, culture and drug susceptibility testing to enhance the diagnosis, control and management of tuberculosis.

The prevalence of MDR-TB recorded in this study is (17.5%) is alarming. This calls for urgent intervention and control measures. The control of tuberculosis especially the MDR-TB involves measures which are aimed at identifying and controlling the sources of infections, protecting people at risk, treatment of infected individuals and public enlightenment.

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REFERENCES

America Thoracic Society (ATS) (1986): Treatment of tuberculosis and tuberculosis infection in adults and children. *Am. Rev. Respir. Dis. 134:* 355 – 363.

Araoye, M.O. (2004): Subjects selection. In; Research Methodology with Statistics for Health and Social Sciences. Araoye, M.O. (ed). Nathadex publisher. pp 115-130.

Borgdoff, M.W., Nagelkerke, N.J.D., Dye, C. and Nunn, P. (2000): Gender and tuberculosis: a comparison of prevalence surveys with notification date to explore sex differences in case detection. *Int. J. Tuberc. Lung Dis. 4*: 123 – 132.

da Silva, P.A. and Ainsa, J.A. (2007): Drugs and Drug interactions. In, Tuberculosis 2007. From Basic Science to patient care. Palomino, J.C., Leao, S.C. and Ritacco, V. (editors). First edition. www.TuberculosisTextbook.com. Pp 593-633.

Dye, C., Williams, B.G., Espinal, M.A. and Raviglione, M.C. (2002): Erasing the world's slow stain: strategies to beat multidrug-resistant tuberculosis. Science 295: 2042-2046.

Eyob, G., Guenbrexabher, H., Lemma, E., Wolday, D., Gebeyehu, M., Abate, G., Rigouts, L., Van Soolingen, D., Fontanet, A., Sanders, E. and Dorigo- Zetsma, J.W. (2004): Drugs susceptibility of *Mycobacterian tuberculosis* in HIV- infected and uninfected Ethiopians and its impact on outcome after 24 months of follow up. *Int J Tuberc Lungs Dis. 8*(11):1388-1391.

Chakraborty, N., De, C., Bhattacharyya, S., Mukherjee, S.S., Benerjee, D., Sarkar, R.N. and Guha, S.K. (2010): Drust susceptibility profile of *Mycobacterium tuberculosis* isolated from HIV infected and uninfected pulmonary tuberculosis patients in Eastern India. *Trans Roy Soc Trop Med Hyg . 104* (3):195-201.

Domingo, J.P. (2007). Tuberculosis and HIV/AIDs. In: Tuberculosis 2007. From basic science to patient care. Palomino, J.C., Leao, S.C. and Ritacco, V. (Editor). 1st Edition. Pp. 559 – 591.

Fujiki, A. (2001): Culture examination for *M. tuberculosis.* In, TB Bacteriology Examination to stop TB. Fujiki, A (ed). Pp 14-19.

Garcia de Viedma, D. (2003): Rapid detection of resistance in *Mycobacterium tuberculosis:* a review discussing molecular approaches. *Clin Microbiol Infect 9:* 349-359.

Grange, J. M. (1998): Tuberculosis. In: Topley and Wilson's Microbiology and Microbial infections. 9th edition Vol. 3. Hausler, W.J. Jr. and Sussman, M. (ed.). Oxford University Press. pp 391 – 417.

Horne, N. (1996): Tuberculosis and other mycobacterium diseases. In: Mandell, G., Douglas, R. and Bennett, J. (ed.) Principles and Practice of Infectious Diseases 3rd edition. New York. Churchill Livingstone. pp 971-1015.

Idigbe, E.O. and Onwujekwe, D.I. (1983): Clinico-Laboratory study of pulmonary tuberculosis in Lagos , Nigeria. *Nig. J. Microbiol. 3:*107-113.

International Union Against Tuberculosis and Lung Disease (IUATLD) (1986): Technical Guide for sputum examination for tuberculosis by direct microscopy supl. 2 IUATLD. Paris.

Itah, A.Y. and Udofia, S.M. (2005): Epidemiology and Endemicity of pulmonary tuberculosis (PTB) in South-Eastern Nigeria. *South Asian J. Trop. Med. Pub Hlth. 36(2):*317-323

Kent, P.T. and Kubica, G.P. (1985): Public Health Mycobacteriology. A guide for the level III laboratory. US Department of Health and Human Services, Centre for Disease control, Atlanta.

Martin, A. and Portaels, F. (2007): Drug Resistance and Drug Resistance Detection. In, Tuberculosis 2007. From Basic Science to patient care. Palomino, J.C., Leao, S.C. and Ritacco, V. (editors). First edition. www.TuberculosisTextbook.com. Pp. 635- 660.

Murray, C.J. and Lopez, A.D. (1997): Mortality by cause for eight regions of the world: Global Burden of Disease Study. *Lancet; 349:* 1269-1276.

National Bureau of Statistics (2006): Federal Republic of Nigeria: 2006 Population Census. www.nigerianstat.gov.ng

Nwachukwu, E. and Peter, G.A. (2010): Prevalence of *Mycobacteria tuberculosis* and human immunodeficiency virus (HIV) infections in Umuahia, Abia state, Nigeria. *Afr. J. Microbiol. Res. 4 (14):* 1486-1490.

Okodua, M.A., Nwobu, G.O., Tatfens, Y.M., Ongey, J.Y. and Agwu, E. (2004): Incidence of HIV-related pulmonary tuberculosis in Edo state, Nigeria. *Shiraz E-Med. J. 5(1):*8-12

Oyesiku, O.O. and Kojeku, G.O. (1992): Abeokuta; In: Ogun State maps. Onakomaya, S.O., Oyesiku, K. and Jegede, F.J. (eds). Rex Charles publication. Pp 153-155.

Palomino, J.C. (2005): Nonconventional and new methods in the diagnosis of tuberculosis: feasibility and applicability in the field. *Eur Respir J. 26:* 1-12.

Rose, R. (1991): Immunology of the lung in HIV infection; the pathophysiologic basis for the development of tuberculosis in the AIDS setting. *Bull. Int. Union Tuberc. Lung. Dis. 99* : 15 – 20.

Schluger, N. W., Harkin, T. J. and Rom, W. N. (1996): Principles of therapy of tuberculosis in the modern era. In: Rom, W. N, Garay, S.M. (eds). Tuberculosis Boston, Little Brown & Co. PP. 751 – 761.

Shao, Y., Yang, D., Xu, W., Lu, W., Sog, H., Dai, Y., Shen, H. and Wang, J. (2011): Epidemiology of antituberculosis drug resistance in a Chinese population: current situation and challenges ahead. *B.M.C. Pub. Hlth. 11:* 110.

Sharma, S.K. and Mohan, A. (2004): Multidrug-resistant tuberculosis. *Indian J. Med. Res.* 120: 354-376.

Stead, W. W. (1992): Genetics and resistance to tuberculosis. *Ann. Intern. Med. 116* : 937 – 941.

Tomford, J.W. (2004): Tuberculosis. The Cleveland Clinic. Sept. 2004.

Ukwandu, N.C.D. (1998): Evaluation of the laboratory techniques used in the diagnosis of sputum-producing patients suspected of mycobacterium infection. *West Afr. J Med. 17:*38-41

W.H.O. (World Health Organisation) (1994): TB – A Global Emergency. *World Health Organisation, Geneva. (WHO/TB/94.177).*

W.H.O. (World Health Organization). (2009): Treatment of tuberculosis: guidelines- 4th edition. *WHO/HTM/TB/2009.* 420.

W.H.O. (World Health Organization). (2010a): Global Tuberculosis Control. WHO Report 2010.

W.H.O. (World Health Organization). (2010b): Multidrug and extensively drug-resistant TB (M/XDR-TB). 2010 Global Report on Surveillance and Response. *WHO/HTM/TB/2010.3.*

AUTHORS' CONTRIBUTIONS

Okodua M., is the main researcher and conducted this study under the supervision of Ihongbe J. and Esumeh F.