## ORIGINAL ARTICLE

AFRICAN JOURNAL OF CLINICAL AND EXPERIMENTAL MICROBIOLOGY SEPTEMBER 2009 ISBN 1595-689X VOL 10(3)

AJCEM/200903/20920 -http://www.ajol.info/journals/ajcem



AFR. J. CLN. EXPER. MICROBIOL 10(3): 175-184

# BRONCHOPULMONARY TUBERCULOSIS- LABORATORY DIAGNOSIS AND DOTS STRATEGY OUTCOME IN A RURAL COMMUNITY: A RETROSPECTIVE STUDY

**[1]Enwuru Chika Paulinus, [2]Emeh Madubuike Samuel, [2]Dr Izuehie Ifeanyi Samson, [3]Enwuru Christian Azubuike, [4]Umeh Sarah I. [5]Agbasi Uchenna Marcel. [1]Department of Medical Microbiology and Parasitology, Nnamdi Azikiwe University, Nnewi campus, Anambra State, Nigeria. [2]Osina Community Hospital, Osina Ideato North, Imo State, Nigeria. [3]Nigerian Institute of Medical Research Yaba, Lagos, NIgeria. [4]Department of Microbiology, Federal University of Technology Owerri, Imo State Nigeria. [5]Department of Science Lab. Technology, Imo State Polytechnic, Umuagwo, Nigeria.**

**CORRESPONDENCE: Enwuru Chika Paulinus. P. O. Box 38, Urualla, Ideato North, Imo State, Nigeria. E-mail: globachik@yahoo.com**

## ABSTRACT

**Pulmonary tuberculosis is still a global public health threat. Despite all efforts at its containment, the scourge is still menacing especially in the rural communities and among HIV infected patients. This retrospective study was carried out to determine the case detection rate of pulmonary tuberculosis in a rural community hospital in Nigeria from 2001-2006. A total of 1219 suspected patients were tested for pulmonary tuberculosis by sputum smear stained by Ziehl-Neelsen technique. Out of this number, 350 (28.7%) were positive for Acid-Fast Bacilli including 198 males and 152 females. Also 235 of the sputum-smear positive patients were tested for the human immunodeficiency virus (HIV) antibodies by Immunocomb 11 HIV 1 & 2 Bispot and confirmed by Immunocomb 11 HIV 1 & 2 Combfirm and HIV-1 Western Blot kit. Sixty three (26.8%) of the sputum-smear positive patients were co-infected with HIV.**

**Two hundred and seventy (77.1%) of the AFB positive patients were treated under the Directly Observed Therapy-Short course, 201 of them (74.4%) completed the treatment, 39 (14.4%) defaulted, 30 (11.1%) died before the completion of the treatment, 195 of the patients were declared cured and 6 were declared failed. Case detection rates could be improved upon by providing culture facilities at the DOTS centers. Also efforts should be made to ensure that all positive cases are followed to a logical conclusion and that anti-retroviral drugs are provided for patients co-infected with HIV to reduce the mortality rate of pulmonary tuberculosis.**

**KEY WORDS: PULMONARY TUBERCULOSIS, HIV, DOTS, AFB.**

## INTRODUCTION

Despite the attention and financial resources it had attracted to itself over the years, pulmonary tuberculosis still remains a major global public health problem. Approximately 2 billion people (one third of the world's population) are already infected with the TB bacillus (1). About 8.8 million new TB cases were estimated in 2005; 7.4 million in Asia and sub Sahara Africa. A total of 1.6 million people die of TB including 195,000 patients infected with HIV (1).

The World Health Organization (WHO) declared tuberculosis a world emergency in 1993 (2). In 2006, Nigeria was ranked as having the fourth largest tuberculosis burden in the world out of 22 high burden countries (3). (India and China ranked first and second respectively (4)). Subsequently, the Federal Ministry of Health declared tuberculosis a national emergency.

In 2005 report, the TB incidence rate was stable or in decline in all six WHO regions, however, the total number of new TB cases was still rising slowly because the case-load continued to grow in Africa, Eastern Mediterranean and South-East Asia regions (5). The recommended strategy was for countries to strive to detect at least 70% of new smear-positive cases and ensure a total cure rate of at least 35% of these detected cases. To achieve this, WHO in 1994 recommended that the national TB programmes adopt the strategy of 'Directly Observed Therapy Short course' (DOTS) (1). The two most important, out of the 5 main components of DOTS being 'improved cases detection by sputum-smear microscopy of symptomatic patients and standardized short-course chemotherapy to all sputum smears positive cases with direct observation of drug intake in at least the first 2 months of treatment' (1). By 2004, 182 countries had adopted and were implementing DOTS in their National programme, and in 2005 it increased to 187 countries (5).

More than 90 million TB patients were reported to WHO between 1980-2005; 26.5 million patients were notified by DOTS programmes between 1995-2005, and 10.8million new smear-positive cases were registered for treatment by DOTS programme between 1994 and 2004 (5).

Globally, WHO reported 2.3 million and 2.1million new smear-positive case notifications and 60% and 65% new smear-positive case detections under DOTS in 2005 and 2006 respectively (5). Under this report WHO reviewed the number of new smear-positive cases successfully treated under DOTS at 1.7 million and 1.8 million in 2005 and 2006 respectively.

The proportion of HIV-positive people screened for TB rose from 8.8% in 2005 to 61% in 2006 and the number of TB cases found to be HIV positive rose from 0.083% in 2005 to 0.5% in 2006 (5).

Presently, above 89% of the world's population lived in areas where DOTS is being implemented by public health services. Global data clearly indicates that most of the resource poor countries are facing some limitations in the implementation of their DOTS programmes (6).

A number of factors contribute to the tuberculosis epidemic in various parts of the world. Severely deficient general healthcare infrastructure is the driving force. Among other factors, poverty (7), ignorance (2) and HIV co-infection (8, 9, 10) stand out as the disturbing pre-disposing factors for the spread of tuberculosis. Previous studies have revealed that HIV infected patients have increased risk for reactivation of latent tuberculosis, of rapid progression to disease of a newly acquired infection, and of death from tuberculosis infection (4, 12, 13, 14). The increase in the number of patients with HIV/TB co-infection has resulted in significant rise in the transmission of multidrug resistant *Mycobacterium tuberculosis* strains (15).

The six principal components highlighted by the 'stop TB strategy' (5), a new global vision include: addressing TB/ HIV co-infection, controlling and combating MDR-TB,

contributing to the strengthening of healthcare system, engaging all healthcare providers, empowering patients and, communities and enabling and promoting research. All efforts are geared towards improving overall global TB control and reduce morbidity and mortality particularly in rural communities such as the one under review.

Several studies in Nigeria in the past two decades have tried to present the picture of the tuberculosis situation in some cities of the country such as Portharcourt (16), Lagos (17, 18, 19), Benin City (20), and Ibadan (21). These were studies based in urban cities. Reports of the TB situation in rural communities of the country with low socio-economic status and poor healthcare facilities, where majority of the patients reside, is scarce.

Therefore, this study was designed to assess the extent of realization of the 2005 global targets of 70% cases detection and 85% cure rate proposed by the WHO assembly in 2000 (22) in a rural community. From this point, we x-ray the need to brace-up to partner with WHO on the policies and strategies to address the major constraints towards achieving global TB control and the primary vision of the stop TB strategy " the global plan to stop TB, 2006-2015" launched in Jan. 2006 (5).

## MATERIALS AND METHODS

### THE STUDY AREA

The assessment was conducted at Osina Community Hospital, a secondary healthcare facility located in Osina, Ideato North Local Government Area of Imo State. The hospital was the only Directly Observed Therapy Short course (DOTS) centre for tuberculosis in Ideato North and South LGAs and a few others nearby LGAs in Imo State as at the time of this study. The presence of German expatriate specialist medical officers from the inception of the hospital up to the late 90's gave the hospital a wide scope of patient in-take from all over Imo State and the neighboring states of Abia, Anambra and Enugu.

The DOTS centre commenced in 1996 and follows the guidelines of the National Tuberculosis/Leprosy Control Programme in conjunction with German Leprosy Relief Association (GLRA).

### THE PATIENTS

All patients attending the out-patients department of the Osina Community Hospital with symptoms of pulmonary disorders either as primary patients or referred from other hospitals and clinics and whose 3 sputum (one spot and two other consecutive) samples were submitted to the lab for testing between Jan 2001 to Dec. 2006 were assessed for this report.

A total of 1219 patients were tested for pulmonary tuberculosis from January 2001 to December, 2006.

### METHOD OF TESTING

Three sputum samples were collected from the patients according to the National Tuberculosis/ Leprosy Control Programme guidelines as follows: 1st spot sample on arrival at the

laboratory, 2nd early morning sample the next day and 3rd sample produced on submission of the 2nd sample. For follow-up laboratory testing of smear-positive patients on treatment, 2 consecutive early morning sputum samples were collected. Smears of the samples were made according to standard procedures (23) and stained by Ziehl-Neelsen technique. The films were thoroughly examined under oil-immersion for the acid-fast bacilli. Patients were classified as smear-positive if at least 2 samples out of the 3 examined were positive for AFB. Culture facilities for *Mycobacterium sp* were not available in the laboratory within this period of review. Patients who have only 1 smear-positive result were asked to repeat the test after a short while. Smear-positive patients were counseled by the medical officer to enroll in the NBTL/GLRA Directly Observed Therapy Short course (DOTS) which includes 2 months intensive phase and 6 months continuation phase. Treatment followed the NBTL/ World Health Organization guidelines.

Patients were re-tested in the laboratory for AFB at the end of the 2nd month, 5th month and 7th month respectively. Treatment outcome for each of the patients was recorded after the final AFB result and completion of the treatment.

**HUMAN IMMUNODEFICIENCY VIRUS (HIV) TESTING**

HIV testing was performed for some of the patients based on the selection criteria of the medical officer. A total of 235 sputum-smear positive patients were co-tested for HIV antibodies. Testing was performed using Immunocomb 11 HIV 1 & 2 Bispot (Orgenics, Israel) and confirmed by HIV-1 Western Blot kit (Epitope Inc, Beaverton, Oregon) and Immunocomb 11 HIV 1 & 2 Combfirm (Orgenics, Israel).

No anti-retroviral drug (ARV) was provided in the treatment centre for HIV-infected Tb patients at the time of the study. With this period under review data for this retrospective study were gathered from the laboratory and clinical case notes of the patients respectively.

**RESULTS**

From January 2001 to December 2006, a total of 1219 patients were tested for pulmonary tuberculosis by the Ziehl-Neelsen staining technique for acid fast bacilli. Out of this number, 350 (28.7%) were positive. This includes 198 (56%) males and 152 (43%) females, male to female ratio 1.3:1. The year 2004 has the highest number of pulmonary tuberculosis patients, 76(21.7%): 39 males and 37 females, followed by the year 2003 with 62 smear positive patients (17.7%): 31 males and 31 females. The year 2005 had the least smear positive patients (43, 12.3%) (Table 1). Mean age of occurrence of pulmonary tuberculosis was 35.4 ± 14.7 years. Peak age frequency was in the age range 20 to 29 (108, 30.9%). This was followed by the age range 30 to 39 (91, 26%) as seen in table 2.

A total of 235 sputum smear positive patients were tested for the HIV antibodies.

**TABLE 1: SPUTUM SMEAR RESULTS AND TREATMENT OUTCOMES**

| YEAR | TOTAL NO EXAMINED | POSITIVE M | F | T | NO TREATED | TREATMENT COMPLETED | CURED | FAILED | DEFAULTED | DIED |
|---|---|---|---|---|---|---|---|---|---|---|
| 2001 | 414(34.0%) | 35 | 24 | 59 | 42 | 31 | 31 | 0 | 8 | 3 |
| 2002 | 179(14.7%) | 29 | 24 | 53 | 43 | 37 | 37 | 0 | 2 | 4 |
| 2003 | 162(13.3%) | 31 | 31 | 62 | 48 | 35 | 33 | 2 | 7 | 6 |
| 2004 | 219(18.0%) | 39 | 37 | 76 | 59 | 41 | 40 | 1 | 9 | 9 |
| 2005 | 135(11.1%) | 25 | 18 | 43 | 28 | 13 | 12 | 1 | 10 | 5 |
| 2006 | 110(9.0%) | 38 | 18 | 57 | 50 | 44 | 42 | 2 | 3 | 3 |
| TOTAL | 1219 | 198 (28.7%) | 152 | 350 | 270 (77.1%) | 201 (57.4%) | 195 (55.7 %) | 6 (1.7%) | 39 (11.1% | 30 (8.6%) |

**M= male**
**F= female**
**T= Total**

Of this, 63 (26.8%) were positive for HIV. There were more female HIV positive patients (34, 54%) than males (29, 46%) Again, the year 2004 had the highest HIV positive tuberculosis patients (20, 35.1%). There were more male HIV positive tuberculosis patients in the years 2001 and 2006 and more females in 2002, 2003 and 2005 (figure 1). Of the 350 sputum smear positive patients, 270 (77.1%) enrolled for the DOTS treatment while 80 (22.9%) did not show up despite extensive counseling by the medical officer. Out of the 270 patients that started the treatment, 201 (74.4%) completed the treatment.

Of those that started the treatment, 39 (14.4%) defaulted and were lost in the study and 30 (1.1%) of those that started the treatment died before completion of the treatment. Of the 201 that completed the treatment, 195 (97%) were declared cured after follow-up sputum smear negative results at the end of treatment while 6 (3%) were declared failed following persistent sputum smear positive results at the end of the treatment period. Out of the 195 that were declared cured, 5 (2.6%) had under one year repeat episodes (i.e. presented back about a year later with recurrent sputum smear positive tuberculosis).

**TABLE 2: AGE DISTRIBUTION OF PULMONARY TUBERCULOSIS PATIENTS.**

| Year | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | Total |
|---|---|---|---|---|---|---|---|
| AGE 10-19 | 7 | 3 | 6 | 6 | 5 | 4 | 31 |
| 20-29 | 19 | 23 | 23 | 13 | 11 | 19 | 108 |
| 30-39 | 13 | 13 | 17 | 23 | 12 | 13 | 91 |
| 50-59 | 5 | 3 | 3 | 6 | 5 | 6 | 28 |
| 60-69 | 4 | 4 | 1 | 11 | 1 | 1 | 22 |

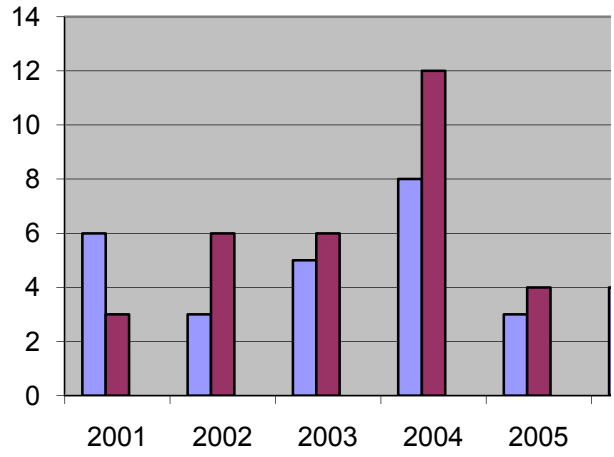


**FIGURE 1: MALE- FEMALE DISTRIBUTION OF HIV/TB CO-INFECTION**

**DISCUSSION**

PTB detection rate of 28.7% was recorded in this study. This was detected by sputum smear. The WHO national case detection rate of pulmonary tuberculosis by sputum smear in Nigeria was 27% in 2004. But it has been reported that pulmonary tuberculosis patients with less than $10^4$ bacilli/ml of sputum cannot be detected by smear AFB microscopy (24). Furthermore, this rate was detected among patients with symptoms of pulmonary disorders. A good number of latent and asymptomatic tuberculosis patients were left undetected. The male-to-female ratio for pulmonary tuberculosis was 1.3: 1. This correlates with the findings of Nwokoma in Portharcourt (16). Several other studies in the country have reported similar higher male pulmonary tuberculosis cases (17, 19) contrary to the findings at Ibadan where it was reported to be higher females than males (21). In the 6 year period, the year 2004 had the highest number of tuberculosis patients (76, 21.7%). This was followed by the year 2003. A cursory look at the WHO data for Africa shows the same trend (3). The mean age of patients infected by tuberculosis in this study was 35.4± 14.7. This falls between the age ranges discovered in Lagos (19) and Portharcourt (16). The peak age frequency was in the age range 20-29 followed by 30-39 years. This was the same peak age discovered in Ibadan (7) and closely related to the findings in Lagos (17) and Portharcourt (16) and corroborates reports that majority of people affected by tuberculosis in the developing countries were below the age of 50 while those of the developed countries were above the age of 50 (17, 25) .

Of the 350 smear-positive patients, 235 were tested for HIV infection. 63 (26.8%) of these were positive. This agrees with the WHO estimate that about 27% of tuberculosis patients in Nigeria were also co-infected with HIV (3), but below the reported finding in Malawi that nearly two-thirds of tuberculosis patients were HIV positive (9). However, the number of patients tested for HIV in this study depended on mere clinical presentations and not a routine measure. This implies that those who were

tested manifested AIDS symptoms. This method of selection is obviously a source of bias since high risk patients could have escaped the clinical acumen of the medical officer. The synergistic effect of HIV/TB co-infection has been on the increase and accounts for more deaths associated with tuberculosis. Unfortunately, in this TB treatment centre, as in many others within some region of Africa, no antiretroviral drug is provided for the HIV infected TB patients. This will definitely compromise the treatment of these patients and could even increase the potential for the transmission of multi-drug resistant (MDR) (10) and extensive drug resistant (XDR) (27) tuberculosis.

As with the age distribution of tuberculosis patients in this study, most of the HIV infected TB patients were in the age range of 20-29 and 30-39. These are the sexually active age groups which are known to be at high risk of HIV infection. Earlier studies have revealed that TB patients less than 50 years of age are more frequently HIV infected (26). There were more female HIV infected TB patients than males, the same trend that was reported in Lagos (17) and Benin City (20) and which the researcher in Benin City attributed to higher female sexual activities. The bio-anatomical nature of female genito- urinary system is also a contributing factor.

Of the 350 sputum smear positive patients, 270 (77.1%) enrolled for the DOTS treatment while 80 (22.9%) absented after counseling. This is worrisome because these people went back into the community without receiving appropriate treatment and continued to shed the bacilli in the environment to the detriment of the general populace. Some of these patients erroneously believe that tuberculosis is 'witchcraft' or 'poison' sent to them by their enemies, relatives or neighbors. They therefore go to seek 'solution' from traditional medicine or 'spiritual houses'. The proprietors of these non-scientific medicine centres give the patients false assurance of spontaneous cure after their rituals and prayers. One of such patients traced was even assured that the blood he was coughing out was a way of getting rid of the 'poison' he swallowed from his 'wicked uncle'. However, this patient was abandoned by this 'miracle worker' when his condition worsened but after two months at the DOTS centre, he made a dramatic recovery. Many of this kind of case abound in these rural communities and some could not muster the courage to come back to the hospital after their initial refusal of treatment, unless compelled by some enlightened relative or friends for the fortunate ones. Some come when it was too late owing to ignorance.

Furthermore, out of the 270 patients that started the DOTS treatment, 201 (74.4%) completed the approved treatment regiment, 39 (14.4%) defaulted (abandoned the treatment) and were lost in the study. This could be as a result of the tendency among many patients especially the less informed in the rural communities to abandon treatment once their health seemed to have improved. Some of these patients could

also have died without proper document. The defaulter-retrieval function of the local government Tb supervisor is not sincerely done due to dereliction of duty by the officer concerned or as a result of paucity of funds, or because the patients or their relatives do not give correct and detailed contact addresses, or the patient may have relocated.

Of those that started the treatment, 30 (11.1%) died before the completion of the treatment. This could be as a result of the delay by patients in seeking medical attention at the onset of the symptoms. The non inclusion of antiretroviral drugs to the treatment regimen of the HIV infected Tb patients could also have caused the death of some of the patients as some of the dead were HIV positive.

Out of the 201 patients that completed the treatment, 195 (97%) were declared cured. This is better than the reported success rates in Nigeria of 79% between 2001 and 2002, 59% in 2003 (3) and the WHO target of 85% in Nigeria at these periods.

Six patients (3%) out of those that completed the treatment were declared failed. These could be patients infected with multidrug resistant (MDR) and extensive drug resistant (XDR) strains of *Mycobacterium tuberculosis* (10, 27), although there is presently no scientific report on MDR/XDR in Nigeria to the knowledge of these authors.

Furthermore, 5 patients (2.6%) of those that were declared cured had repeated episodes. This is quite alarming and could be endogenous reactivation of the previous tuberculosis or exogenous re-infection of the patient (28). Previous studies have noted that patients cured of Tb infection by one strain of *Mycobacterium tuberculosis* could be re-infected by another strain as the immunity by the primary strain does not protect the patient against a later infection by another strain (3). Rate of re-infection has been reported to be higher than that of new infections in South Africa (29).

**RECOMMENDATION AND CONCLUSION**

From the results obtained in this study, it could be seen that the global targeted case detection and cure rates are achievable even in the rural areas with a little more efforts. An improvement in the case detection rate could be achieved by provision of culture facilities at the DOTS centre or at a nearby referral centre. Defaulter retrieval should be intensified through provision of adequate funds to provide incentives to local retrieval officer and to mobilize the patients to visit the clinic days this will save the community from being infected by fleeing infected patients who hide in the village and continue to shed the infective bacilli to the environment. Antiretroviral drugs must be provided for HIV infected Tb patients to reduce the death rate attributed to tuberculosis. Apart from the radio and television jingles on Tb, other means of enlightenment of the people in the rural areas should be adopted such as house to house visitation by the local authorities and rallies at the village squares to let the people know what tuberculosis is and what it is not in order to reduce morbidity, mortality and stigma

otherwise the global emergency is yet to commence.

**REFERENCES**


1. World Health Organization: Global Tuberculosis Central, Surveillance planning financing. WHO Report, Geneva, 2005 (WHO/HTM/TB/2005. 349).
2. Davies P.D. Tuberculosis: The global epidemic. *J Indian Med Assoc*. 2000; **98 (3**): 100-2
3. World Health Organization: Global tuberculosis control: WHO Report. Geneva: The Organization; 2006.
4. World Health Organization: Global tuberculosis control; Surveillance, planning, financing. Geneva: The Organization; 2005.
5. World Health Organization Global Tuberculosis control Surveillance planning, financing WHO Report, Geneva 2007 (WHO/HTM/TB/2007.376).
6. Idigbe E.O. Contemporary global strategies for TB control. *Nigeria Journal of Clinical and Biomedical Research* 2006: 1; 6-7.
7. Nwachokor F.N., Thomas J.O. Tuberculosis in Ibadan, Nigeria- a 30 year review. Cent Afr J Med. 2000**; 46 (11**): 289-92.
8. Frieden T.R., Sterling T.R., Munasiff S.S., Watt C.J., Dye C. Tuberculosis. *Lancet*. 2003; **362**: 887-99.
9. Crampin A.C., Glynn J.R., Traore H., Yates M.D., Mwaungulu L., Mwenebabu M., Chaguluka S.D., Floyd S., Drobniewski F., Fine PEM. Tuberculosis transmission attributable to close contacts and HIV states. *Emerg Infect Dis*. 2006; **12(5**): 729-35.
10. Haar C.H., Cobelens F.G.J., Kalisvaart N.A., van der Have J.J., van Gerven P.J.H.J., van Soolingens D. Tuberculosis drug resistance and HIV infection. *Emerg Infect Dis*. 2007; **13(5**): 776-8.
11. Selwyn P.A., Hartel D., Lewis V.A., Schaenbaum E.E., Vermund S.H., Klein R.S., Walker A.T., Friedland G.A. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. *N Engl J Med*. 1989; **320**: 545-50.
12. Dally C.L., Small I.M., Schecter G.F., Schoolnik G.K., McAdam R.A., Jacobs W.R., Hopewell P.C. An outbreak of tuberculosis with accelerated progression among persons with human immunodeficiency virus. An analysis using restriction-fragment-length polymorphisms. *N Engl J Med*. 1992; **326**: 231-5.
13. Di perri G., Cruciani M., Danzi M.C., Luzzati R., De C.G., Malena M., Pizzighella S., Mazzi R., Solbiati M., Concia E., Basetti D. Nosocomial epidemic of active tuberculosis among HIV infected patients. *Lancet*. 1989; **2**: 2502-4.
14. Mukadi Y.D., Maher D., Harris A. Tuberculosis case fatality rates in high HIV prevalence populations in sub-Saharan Africa. *AIDS*. 2001; **15**: 143-52.
15. Balcells M.E., Thomas S.L., Godfrey-Faussett P., Grant A.D., Isoniazid preventive therapy and risk for resistant tuberculosis. *Emerg Infect Dis*. 2006; **12(5**): 744-51.

16. Wokoma F.S. Trends in case occurrence of pulmonary tuberculosis in Portharcourt Teaching Hospital-a five year analysis of admissions. *Nigerian Medical Practitioner* 1999; **37(314)**: 41-3.
17. Idigbe E.O., Nasidi A., Anyiwo C.E., Onubogu C., Alabi S., Okoye R., Ugwu O., John E.K.O. Prevalence of human immunodeficiency virus (HIV) antibodies in tuberculosis patients in Lagos, Nigeria. *J Trop Med Hyg*. 1994; **97**: 91-7.
18. Enwuru C.A., Idigbe E.O., Ezeobi N.V., Otegbeye A.F. Care-seeking behavioral patterns, awareness and diagnostic processes in patients with smear- and culture-positive pulmonary tuberculosis in Lagos, Nigeria. *Trans R Soc Trop Med Hyg*. 2002; **96**: 614-6.
19. Odusanya O., Babafemi J.O. Patterns of delays amongst pulmonary tuberculosis patients in Lagos, Nigeria. *BMC Public Health*.2004; **4**: 18.
20. Uche A., Alozie K.O. Changing prevalence of HIV among pulmonary tuberculosis patients in Benin City, Nigeria. *Int Conf Aids*. 2004; **15**. Abstr no TuPeD 5203.
21. Ige O.M., Bakare N.A., Onadeko B.O. Modified short course chemotherapy of pulmonary tuberculosis in Ibadan, Nigeria- a preliminary report. *Afr J Med Med Sci.* 2000; **29(1)**: 51-3.
22. Stop Tuberculosis Initiative Report by the Director General Fifty-third WHO Assembly. Geneva, 15-20 May 2000 (A53/5, 5).
23. National tuberculosis and leprosy control programme. Workers manual. Federal ministry of health Lagos.1991.
24. Hobby G.C., Halman A.P., Iseman M.B., Jones J.M. Enumeration of tubercle bacilli in sputum of patients with pulmonary tuberculosis. *Antimicrob Agents Chemother*. 1993; **4**: 94-194.
25. Sudre P., Damten G., Kochi A. Tuberculosis: a global review of the situation today. *Bull*. WHO 1992; **70**: 149-292.
26. van der Werf M.J., Yegorova O.B., Chentsova N., Chechulin Y., Hasker E., Petrenko V.I., Veen J., Turchenko L.V. Tuberculosis-HIV co-infection in Kiev city, Ukraine. *Merg Infect Dis*. 2006; **12(5**): 766-8.
27. Centers for Disease Control and Prevention: Revised definition of extensively drug resistant tuberculosis *MMWR Morb Mortal Wkly Rep*. 2006; **55**: 1176.
28. Verver S., Warren R.M., Beyers N., Richardson M., van der Spuy G.D., Borgdorff M.W., Enarson D.A., Behr M.A., van Helden P.D. Rate of re-infection tuberculosis after successful treatment is higher than rate of new tuberculosis. *Am J Respir Crit Care Med*. 2005; **171**: 1430-5.
29. Sonnenberg P., Murray J., Glynn J.R., Shearer S., Kanbashi B., Godfrey-Faussett P. HIV-1 and recurrence, relapse and reinfection of tuberculosis after cure: a cohort study in South African mine workers. *Lancet*. 2001; **358**: 1687-93.