The Growing Burden of Tuberculosis in Nigeria: trends of the disease prevalence and treatment outcome in Enugu state

A thesis submitted to the Center for International Health University of Bergen, in partial fulfilment of the requirement for the award of the European Master of Science in International Health

By

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DECLARATION

Where other peoples work has been used (either from a printed source, internet or any other source) this has been carefully acknowledged and referenced in accordance with departmental requirements.

The thesis “The Growing Burden of Tuberculosis in Nigeria: trends of the disease prevalence and treatment outcome in Enugu state” is my work.

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Total word count: 10,655

DEDICATION

The thesis is dedicated to my dear wife Ngozi, and our lovely children Chidi, Chukwuma, and Amarachi, for their love, support and understanding through out the period of the programme.

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Finally, I give thanks and praises to God Almighty, the giver of life for maintaining my mental/physical health and that of the family during the year long academic pursuit.

Dim CC

ABBREVIATIONS

AFB - Acid-fast bacilli

Anti-TB - anti-tubercular

BCG - Bacille Calmette Guerin

DOTS - Directly Observed Therapy Short-course

DST - Drug sensitivity testing

E - Ethambutol

FDC - Fixed-dose combination

FMOH - Federal ministry of health

H - Isoniazid

HIV/AIDS – Human immunodeficiency virus/Acquired immune deficiency syndrome

LGAs - Local government areas

MDR-TB – Multi-drug resistant tuberculosis

NTBLCP - National tuberculosis and leprosy control programme (of Nigeria)

PHC - Primary health care

PPM – Public-private mix

PTB – Pulmonary tuberculosis

R - Rifampicin

S – Streptomycin

Smear -ve – sputum smear negative

ss+ - sputum smear positive

TB - Tuberculosis

UN - United Nations

WHO – World Health Organization

Z - Pyrazinamide

ABSTRACT

Background: The burden of tuberculosis in Nigeria is the third highest in the world. The data from the TB programme of the States' ministries of health are usually unpublished which possibly contributes to the prevailing ignorance and poor attitude of Nigerians to the disease.

Objectives: To determine the trends of TB burden and treatment outcome in Enugu state; and compare the State's disease burden to that of the Nation.

Methods: The study was a quantitative action research of secondary data from the TB control programme, Ministry of health, Enugu state, the National annual report of 2008, and WHO TB database within the 10 year period of 2000-2009. Data analysis and presentations were descriptive.

Results: The modal age group for new ss+ PTB cases in Enugu state was 25-34 years .The number of female cases was higher than males within the 0-14 year ager group. The annual number of all TB cases showed a raising trend from 914 cases in the year 2000 to 1684 in 2009; but, the reported new ss+ PTB cases fluctuated in a wave-like pattern. The median number of extra-pulmonary TB cases for 2005-2009 was 150 cases while that for the period 2000-2004 was 36 – a four fold increase.

The mean prevalence of HIV for all TB cases and new ss+ PTB were 34.4% and 30.7% respectively for the period 2008-2009. Also, the median treatment success rate was 82% (range: 78-85).

On the average, Enugu State contributed 1.77% of all TB cases and 2.10% of new ss+ PTB to the national annual TB register and a TB case reported in Enugu state was more likely to be a new ss+ PTB when compared to the whole nation [$P < 0.001$, OR = 1.33 (95% CI: 1.26, 1.40)]

The possible impediments to TB control programme in the State include inadequate funds, ignorance and health seeking pattern of the residents, lack of confidence in the public health care delivery system, non-compliance of private medical practitioners to the approved TB treatment guidelines.

Conclusion: Though the burden of TB in Enugu state had increased over the study period, the State's contribution to the disease burden in Nigeria is low. Community participation in TB control and PPM, among other recommendations, will improve TB case detection and treatment in the State.

INTRODUCTION

Tuberculosis(TB) is an infectious disease whose scourge has been with humans throughout known history.[1] About one third of the over 6 billion world population is estimated to be infected with the disease causing organism, and the lifetime risk of developing the disease, for each person, can be over 10%.[2] It is therefore a global pandemic whose impact on world development is well recognized which made the United Nations (UN) to define TB-specific indicators for monitoring her target of reversing the incidence of major diseases by the year 2015.[3] Though TB is curable, about 4500 people die of the disease daily and it is noteworthy that most of these deaths occur in developing countries where poverty, malnutrition, and HIV/AIDS are also prevalent.[4] In response to the huge burden of TB, a major effort towards global control of the disease was initiated through the widespread implementation of the *DOTS* strategy, and this effort is being consolidated and enhanced through the *Stop TB Strategy*.[5] The four main targets of this global control are: the fall of TB incidence by the year 2015; the reduction of TB prevalence and death by half by 2015 when compared to their levels in 1990; the detection and treatment of at least 70% of the estimated incident cases in DOTS programme; and finally, the successful treatment of at least 85% of incident smear-positive cases.[6]

The UN has described the prevalence and deaths from TB as better sensitive indicators of the changing burden of disease[3] therefore, the global TB control efforts could be viewed as successful because the recent WHO report has predicted that TB prevalence and deaths would be halved in three out of the six WHO regions by the target year.[6] However, Africa in general and Nigeria in particular may not be sharing in the global success story – Africa contributed 33% of estimated prevalent cases in 2007 while Nigeria contributed 460,000 cases thereby ranking 4th in the global list of high disease burden countries.[6]

Nigeria is a very populous nation that is divided into several administrative units (States) with varying ethnicity, socio-economic and health indices. How much of the reported national TB burden that is contributed by each State is rarely known to the public, and this may be contributing to the prevailing inappropriate care seeking behaviour and poor awareness of the disease in Nigeria.[7]

STUDY JUSTIFICATION

The ultimate target of the *Stop TB partnership* is to eliminate TB as a public health problem (less than 1 case per million population) by the year 2050.[8] On the other hand, Nigeria is a setting where several health care options (medical pluralism)[9] including orthodox medicine (public, private, or drug stores), traditional medicine, spiritual healers etc; the public health facilities within which the TB control programme operates is "distanced" from the people and are often not the first choice during health seeking decisions. Therefore, for the above target to be achievable in Nigeria using the current passive detection strategy, the people at the community level should be empowered to partner with the TB control objectives through adequate knowledge of the growing burden of the disease and the accessible potentials for cure. As earlier stated, data on TB burden from the States of Nigeria are not published and Enugu state is not an exemption. The TB data reposited with the various States' ministries of health appear to be meant only for generating national estimates and reports. It is argued that if information on the magnitude of TB burden generated from DOTS centers are fed back to the people through the existing community structures such as women meetings etc, detection rate of TB in Nigeria will increase remarkably and the reported TB burden may approach the true population figures. This argument is supported by a recent study which showed that the average delay by patients in southern Nigeria (including Enugu state) before presenting to DOTS centers was 3 months, and the main reason for the poor use of DOTS facilities was ignorance.[7]

Furthermore, TB is linked to poverty and HIV/AIDS. Residents of Enugu state are predominantly poor and the HIV prevalence in the State is the highest among the five South-eastern States of Nigeria.[10] It follows therefore, that the reported TB burden in the State may contribute significantly to the national figures, otherwise gross low detection of

the disease could be suspected. So, it became important to study the changing burden of TB in the State in relation to the national burden. Also, in other to protect the vulnerable population of the State from tuberculosis, as stipulated in the *Stop TB Strategy*, the State's ministry of health would be encouraged to disseminate the study results and also adapt them for use in community partnership towards TB control.

AIM AND OBJECTIVES

Aim

- To determine the trends in the prevalence, incidence, and treatment outcome of tuberculosis in Enugu state, South-eastern Nigeria from 2000 to 2009

Specific objectives

- To determine the trends of the reported annual TB prevalence, TB incidence, and new smear positive PTB in Enugu state of Nigeria, over a ten year period of 2000 to 2009
- To determine the treatment outcome of cohorts of incident smear-positive TB in Enugu state of Nigeria, within the same period.
- To compare trends of the reported TB prevalence and incident smear positive PTB in Enugu state from 2004 to 2008, to the Nigerian national trends over the same period.
- To determine the possible factors militating against TB control in Enugu state and proffer recommendations

LITERATURE REVIEW

Aetiology of TB

TB is caused by the infection with tubercle bacilli - a generic name that incorporates an expanding list of *Mycobacterium* species collectively called *Mycobacterium tuberculosis complex*. Members of this group are: *Mycobacterium tuberculosis, M. bovis, M. africanum, M. microti, M. canetti, M. caprae, and M. pinnipedi.*[11;12] They are generally facultative intracellular (phagocytes) pathogens which may be related to their long period of persistence in individuals with latent TB.[12] Also, they are obligate aerobes therefore; grow better in oxygen rich tissues such as the lungs which may explain why majority of the disease involves the lungs. However, despite their high degree of DNA similarity, *M. tuberculosis* is the major cause of human tuberculosis.[13] Molecular typing of *M. tuberculosis complex* among TB patients in Nigeria showed that majority of the disease was caused by *M. tuberculosis* followed by *M. africanum,* while *M. bovis* contributed the least.[14]

History of TB

TB seams to have been a global public health problem for many centuries as shown by its global afflictions and impacts.[1] Despite the lack of archaeological evidence, the causative organism is hypothesized to have originated from East Africa.[1] Nevertheless, the identification of classical skeletal features of the disease,[15] and the amplification of *M. tuberculosis* DNA[16] in Egyptian mummies are pointers to the possible devastating impact of the disease in ancient Africa.

The isolation of the tubercle bacillus in 1882 by Robert Koch gave hope to the control of an almost evasive disease. Furthermore, the development of streptomycin, isoniazid, and rifampicin in the mid 20th century introduced a new and effective regime for treatment of

TB; prior to then, several treatment strategies with unconfirmed effectiveness such as rest (in sanatorium), exercise, and pulmonary collapse strategies, had been employed.[1;17]

The only available vaccine for TB is *Bacille Calmette Guerin* (BCG). It is made of live attenuated *M. bovis*, and was first used in 1921.[18] Incidentally the vaccine neither prevents primary infection nor the reactivation of latent pulmonary infection which makes it useless for the much needed primary prevention of TB.[19]

Furthermore, the DOTS was introduced in Nigeria in 1993 by the *German tuberculosis/leprosy Relief Agency* (GLRA), and implementation was expanded to all States of the Federation in 2004.[20]

Transmission of TB

TB is a chronic infection with predilection for the human lungs (pulmonary TB) but, it can affect any other organ of body (extra-pulmonary TB).[20] The causative organisms are transmitted through the inhalation of airborne droplet nuclei generated from individuals with the pulmonary disease.[21] Following the infection, any of these outcomes may result thus: the bacilli may be killed by the host immune system; they may proliferate and cause primary TB; they may be dormant and remain asymptomatic (latent infection); or they may be reactivated after a period of latency.[22] It is estimated that about 5-10% of persons with latent infection will develop TB during their lifetime but the risk is higher among children and the immunocompromised such as HIV/AIDS.[21] Also, an average of 10-15 persons are estimated to contract the infection annually from one infectious pulmonary TB case.[19]

A lot of host and environmental factors interact to predispose individuals to TB; the independent risk factors identified in West Africa include family history of TB, household crowding, male sex, HIV infection, smoking - the latter had a dose-response relationship with TB,[23] and therefore should stimulate further studies. A related study in

Gambia had also identified ethnicity as a risk factor but explained that it could be due to the underlying environmental and behavioural factors.[24] Furthermore, a recent study from Tanzania showed that though patients with prolonged duration of cough (two or more weeks) had a higher likelihood of being diagnosed with TB when compared to those with shorter duration of cough, the relationship was not significant [OR = 1.6 (95% CI: 0.59, 4.49)].[25] In Nigeria, the inefficient health system is believed to be perpetuating the cycle of disease-poverty-disease of majority of Nigerian,[26] and this theory definitely applies to TB.

Diagnosis of TB

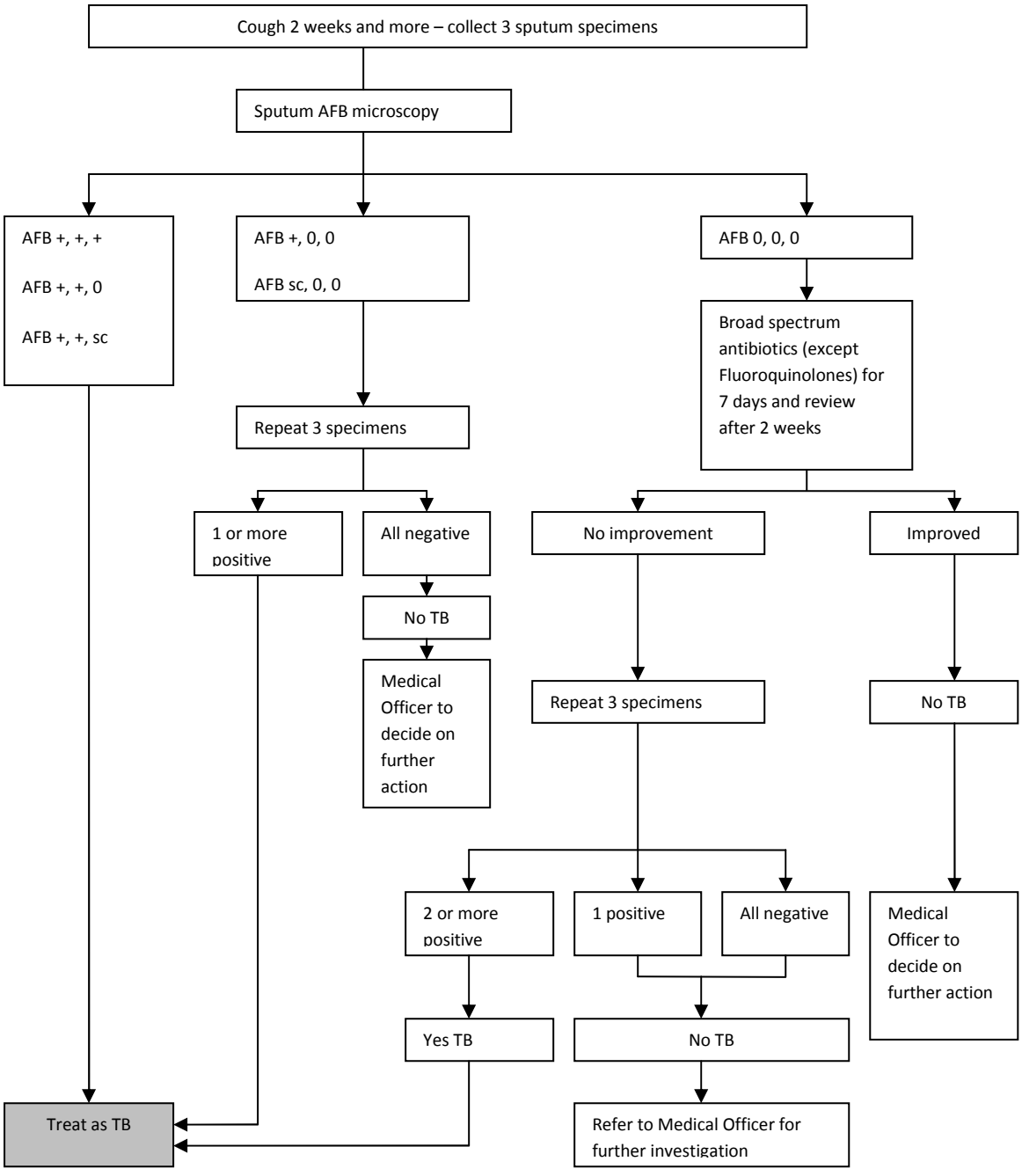
TB can affect any organ of the body but the pulmonary TB especially the reactivated latent infection is of most public health concern because it is the major source of tubercle bacilli spread in the communities.[19] Further reviews will therefore be restricted to PTB.

Generally, the diagnosis of TB is based on "possible exposure, a typical disease history, suggestive clinical findings, typical radiological changes and positive bacteriological tests."[19] Sputum smear direct microscopy and conventional solid media culture are the most widely used laboratory diagnostic methods in the global TB control. However, most diagnoses of TB are based on the smear microscopy for acid-fast bacilli (AFB). The technique is fast, accessible, and specific but it is limited by its low and variable sensitivity and the inability to detect drug resistant bacilli.[27] Because of the progressive improvement of the quality assurance programmes for smear microscopy, WHO has redefined a new sputum smear-positive PTB as the presence of single AFB in at least one sputum smear examination from a TB suspect.[27] Likewise, the number of smears required for the diagnosis of PTB has been reduced to two.[27] This decision considered the barriers of accessing TB control services in resource poor setting including laboratory workload, as well as the incremental diagnostic yield of 3 serial sputum specimens; and hoped that

the new policy would enhance case detection through improved "quality of service, decreased time for diagnosis and initiation of treatment and decreased patients drop out from the diagnostic pathway".[27]

The national tuberculosis programme in Nigeria relies on direct microscopy for diagnoses of PTB (Fig. 1), and is yet to adopt the new WHO policy on new smear positive PTB.[28]

Figure 1: A flow chart for the management of TB suspects in Nigeria.[28]



Key:
+: - positive sputum result expressed in grades 1+, 2+ or 3+;
Sc: - means a scanty positive sputum result;
0: - a negative sputum result

Treatment of TB

BCG vaccination and chemoprophylaxis are unsatisfactory TB control measures thereby leaving anti-tubercular (anti-TB) chemotherapy as the only option.[29] The essential (first-line) anti-TB drugs are isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E), and streptomycin (S).[5] Their use in combinations (multi-drug therapy) is aimed at achieving cure without relapse, preventing death, impeding transmission by depleting infection source pool, and preventing the emergence and transmission of drug resistance.[5;29] The fixed-dose combinations (FDCs) have equivalent efficacy to separate-tablet combinations[30] and are therefore preferred because of several advantages such as increased patient acceptance, discouragement of selective ingestion of the drugs and possible monotherapy, and prescription error.[5] Other strategies introduced to improve TB treatment are the "patient kit" which ensures that the full treatment for a patient is available for the desired treatment duration; the "standard regimen" which introduced a standard (same) treatment for each patient registration group (category).[5]

The standard therapies of TB are usually divided into 2 phases, an initial intensive phase followed be a continuation phase. For new patients, the regime (2HRZE/4HR) consists of an intensive phase of rifampicin, isoniazid, pyrazinamide, and ethambutol daily for 2 months, and a continuation phase of rifampicin and isoniazid for a further 4 months, preferably daily or 3 times per week.[5] Thrice weekly regime through out the course of the treatment is an acceptable alternative in non HIV-prevalent areas provided that treatment is directly observed.[5] This therefore implies that Nigeria with an HIV/AIDS prevalence rate of 3.1% as at 2007,[31] is not eligible to use this alternative regime. Furthermore, in settings with proven or unknown isoniazid resistance level, HRE instead of HR should be used at the continuation phase. The isoniazid resistance status (new cases) of Nigeria is assumed to be low. This is supported by a very small sample study from Jos, northern

Nigeria which did not identify isoniazid resistance in both new and follow-up cases.[32] Nevertheless, this report contrasts an earlier and equally small sample study from a similar region which reported an isoniazid resistance of 6.6% among new cases.[33]

The DOTS in Nigeria uses 2HRZE/4HR or 2HRZE/6HE regimes for category 1 (new cases) – 6HE is self administered while 4HR therapy should be observed daily.[28] For retreatment cases (category 2), the 2SRHZE/1RHZE/5RHE is used.[28] The current WHO guideline recommends that all re-treatment cases undergo specimen culture and drug sensitivity testing (DST) for at least isoniazid and rifampicin before treatment if the Rapid molecular-based DST is available; otherwise standard empirical treatment (category 2) should be commenced and modified with the result of the conventional culture when available.[5] The recommendation is in response to the report of the *Global Project on Anti-tuberculosis Drug Resistance Surveillance* which showed a high global mean multi-drug resistance (MDR) of 15.3% [95% CI: 9.6-21.1] for previously treated cases when compared to 2.9% [95% CI: 2.2-3.6] among new cases.[34] For the African region, the report showed a mean MDR of 1.5% [95% CI: 1.0-2.0] for new cases, and 5.8% [95% CI: 3.9-7.7] for previously treated cases.[34] This apparent low level of MDR-TB gives hope to the control of TB in this continent where poverty, hunger and HIV are endemic. However, the current workers' manual used in Nigeria suggests that the WHO recommendation is only observed after treatment attempts at the category 2 level:

> "for patients who remain positive after category 2; continue RHE medication, inform the Local government TB supervisor (LGTBLS) or State TB control officer (STBLCO), and refer to medical officer for sputum culture, sensitivity test and appropriate treatment"[28]

MDR-TB in Nigeria is apparently low - the estimate for 2007 was 1.8% for new cases and 9.4% for retreatment cases.[6] Also, the study in Jos, reported an MDR of 4% among

new cases and 18% among the follow-up cases,[32] while another study from a referral center in Ibadan, South-western Nigeria showed an MDR of 53.6% among new patients though over half of the cases were from the anti-retroviral clinic of the hospital.[35] The obvious disparity between the two studies calls for a well designed nationwide survey to determine the true picture of anti-TB drug resistance.

On the other hand, a study in Enugu, Nigeria among chronic TB patients referred by the national TB programme for category 2 related problems (failure, relapse, and returning defaulter with smear positive result), showed an MDR-TB of 72%, and poly-drug resistance of 25.6% while one patient each showed sensitivity to all drugs and isoniazid mono-resistance respectively.[36] The study however has questionable internal validity because 33% of the study participants were excluded from analysis for various reasons.[36]

Global burden of TB [6]

According to the WHO estimates for 2007,[6] all incident cases of TB was 9.27 million as against 9.24 million in 2006, and 6.6 million in 1990. Most of the cases were from Asia (55%) and Africa (31%) while the least estimate was from the Americas (3%). Fifteen percent of the 9.27 million incident TB cases were co-infected with HIV and Africa contributed 79% of them. The high burden of TB in Asia and Africa is reflected on the WHO list of high TB burden countries which was topped by five countries from these regions.

The estimated prevalent cases decreased from 13.9 million (210 per 100 000 population) in 2006, to 13.7 million (206 per 100 000 population) in 2007. Also, the estimated deaths from TB was 1.3 million among HIV-negative new TB cases (20 per 100 000 population) and 456 000 among new TB cases who were HIV-positive. Half a million TB cases were estimated to be MDR-TB in 2007; and by the end of 2008, 55 countries had reported extensively drug resistance TB (XDR-TB).

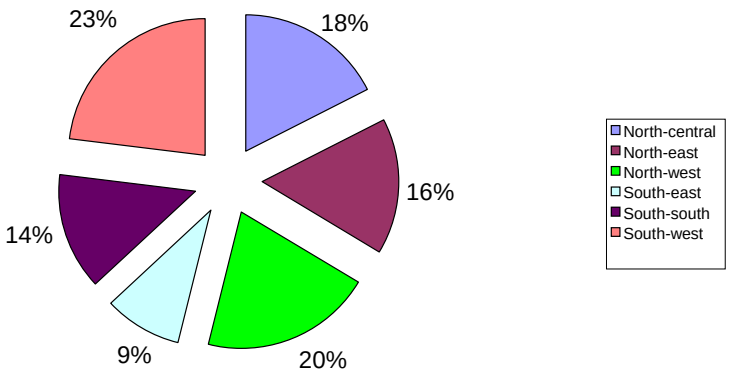
The case detection rate for new smear-positive cases for 2007 was 63% which was still lower than the DOTS target of 70%.

National burden of TB

In year 2007, Nigeria ranked fourth in the world and first in Africa with respect to the WHO estimated number of TB cases.[6] Unfortunately, a 2008 report estimated the total TB cases in Nigeria as 922,575, and was ranked 3rd (behind India and China) on the list of high-burden countries.[37] Furthermore, as at 2007, the WHO estimated that Nigeria had 460,000 cases of all forms of TB, a TB prevalence of 521/100,000 population, 195,000 new smear positive cases, incidence rate (all cases) of 311/100,000 per year, and incidence rate (new smear positive) of 131/100,000 per year.[6] Further estimates include the prevalence of all forms of TB in HIV of 42/100,000, and a death rate of 93/100,000 population per year (138,000 deaths/year).[6]

However, the most recent national TB report[20] showed that since 2002 when nation-wide expansion of DOTS started, only 455,552 of TB (all forms) have been registered; out of which 92.2% were new cases and 7.8% were retreatment cases. In 2008, a total of 90,311 TB cases (92% new cases, 8% retreatment cases) were registered; notably, the sputum smear positive (ss+) cases contributed only 51% of the new cases. The reported new ss+ PTB cases represented only 30.5% of the estimated new ss+ for the year but, nearly doubled the detection rate of 16 % in 2002. The TB cases per State of the Federation for the same year, ranges from 721 cases in Ekiti to 9,864 cases in Lagos. The South-eastern zone to which Enugu state belongs, contributed the least (9%) cases (Fig. 2).

Figure 2: Annual TB cases by zones of Nigeria for year 2008[20]



National TB control programme of Nigeria[20]

The national TB control activities in Nigeria are coordinated by the *National tuberculosis and leprosy control programme* (NTBLCP) which was launched in February 1991 under the department of Public health in the Federal ministry of health (FMOH). Its basic disease control strategy is the provision of free services to all patients identified with TB and its operations are guided by DOTS strategies and *STOP TB Partnership* initiatives.

NTBLCP is structured along the three tiers of Nigerian government thus the Federal, State, and Local government areas (LGAs). Each level provides technical and management support to the one directly below it for instance, the Federal (National) programme supports the States' TB control programme. Furthermore, the Federal level is also in charge of policy development, tertiary patient care, mobilization and development of human and material resource. The States' TB programmes are responsible for coordinating TB control activities within the States, and provision of secondary patients' care. The operational level of the national TB control programme is the LGAs and it is based on the principles of Primary health care (PHC). At least 2 health centers in each of the 774 LGAs in Nigeria have fully functional DOTS services.[6]

NTBLCP re-defined its strategies in 2006 and developed the following specific targets to be achieved by this year - 2010:

- to detect 70% of the estimated smear positive TB
- to successfully treat at least 85% of all detected TB cases
- to ensure a minimum of 80% implementation rate of the programme's activities by strengthening the technical and managerial capacity of the NTBLCP
- to promote behavioural change in the community about TB such that 70% of adult population become aware of TB, its prevention, and the available free treatment as well as motivate the at risk groups to seek for immediate care
- To reduce the incidence of TB among HIV patients by 25%

METHODS

Study setting

The Federal Republic of Nigeria is made up of 36 States and these States are grouped into 6 geo-political zones (Fig. 3). The States are further divided into smaller administrative units called LGAs and there is a total of 774 LGAs in the country. Nigeria is the most populous nation in Africa with a projected population of 149,229,090 million and population growth rate of 2.0% for year 2009.[38]

Enugu state is one of the five States in the South-eastern zone of the country and it has an approximate land mass of 8,727.1 square kilometres (Fig. 3).[39] The State capital is Enugu which is about 5 hours drive from Abuja the capital of Nigeria. The population of the State during the 2006 census was 3,257,298 million;[40] however, with an estimated population growth rate of 2.28% ,[26] the mid year population for 2010 would be 3,564,679. About 95% of the State's population are ethnic Igbos and most of the existing 17 LGAs (Fig. 4) are rural with majority of the working population being farmers and petty traders [26] There is high fertility rate of 5.6, and the average family size is large with a range of 8 to 12 persons per household.[26] The life expectancy at birth is 51 years while the crude death rate is 18 per 1000 population.[26]

The health care services in the State are delivered by private and government (public) health facilities. The latter includes the PHC facilities which are the responsibility of the LGAs, and the secondary care facilities which are managed by the State government. The government health care delivery services were rated as poor to fair by participants in a community survey.[26] The private for-profit hospitals are mostly used by the community, while the PHC facilities which are the operational sites of the DOTS are the least patronized.[26] Furthermore, the accessible recent National HIV sentinel survey showed

that Enugu state had an HIV/AIDS prevalence of 6.5% which was the highest in South-eastern zone of the country.[10]

The State has DOTS services in all the 17 LGAs of the State with a total of 95 functional DOTS and 30 microscopy centres.[20]

Figure 3: Map of Federal Republic of Nigeria[41]

Study design

The study was a retrospective and quantitative research of unpublished secondary data from the TB control programme of the Ministry of health, Enugu state, Nigeria. The data source was the annual registration for TB from all the DOTS centers in the State. All available data on the number of TB cases of all categories registered annually (cohorts), the treatment outcome for the cohorts of new ss+ cases, the HIV prevalence per cohort of TB cases, as well as the age and sex distribution of incident ss+ cohorts for the period 2000 to 2009, were included in the study.

Supplementary data for the national TB prevalence and new ss+ PTB for 2004-2008 were retrieved from the WHO online global TB database[42] and the 2008 annual report of the NTBLCP.[20] Because DOTS became nationwide in 2004, retrieval of national data was restricted to 2004. The 2009 data for the national TB was not available.

Microsoft Excel 2003 computer software was used for data analysis. Data presentation was basically descriptive using tables and charts. However, Epi Info software version 3.5.1 was used where applicable for inferential statistics at 95% confidence level and results were expressed using odd ratios (OR) and P-values. A P-value of less than 0.05 was considered statistically significant.

Possible impediments to TB control in Enugu state were identified through in-depth search for related literatures from the State and similar areas in Nigeria using the following online search engines *African journal online, Google scholar,* and *PubMed.* The e-library of the University of Bergen, and *HINARI* were used to download non-free articles.

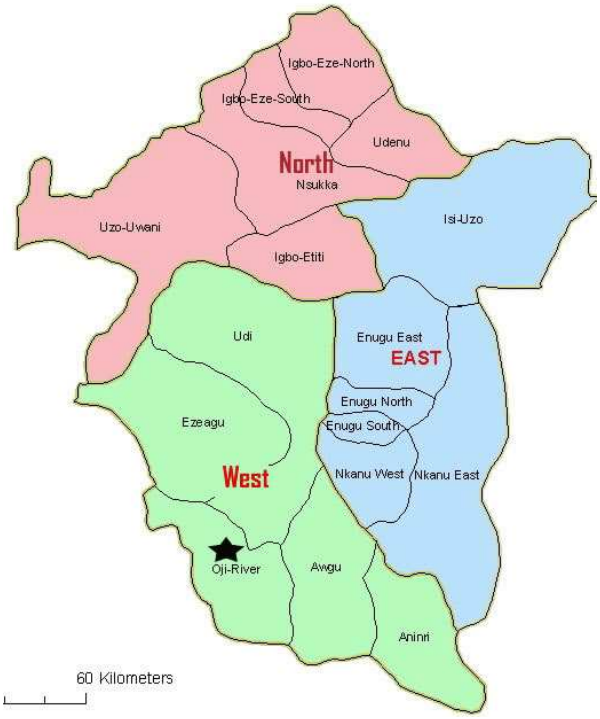


Figure 4: Map of Enugu state, South-eastern Nigeria[43]

Main definitions

The definitions for different categories of TB patients and the treatment outcome by the national TB control of Nigeria are listed below (Tables 1 and 2):

Table 1: Definitions for registered sputum smear positive TB patients in Nigeria.[28]

Category	**Definition**
New case	A patient who has never had treatment for TB or who has taken anti-TB drug for less than 4 weeks.
Relapse	A TB patient who previously received treatment and was declared cured or completed a full course of treatment and has once again developed sputum smear-positive TB
Treatment failure	A smear positive patient who while on treatment remained, or became smear positive again *five months or later* after starting treatment
Treatment after default	A TB patient who completed at least four weeks of Category 1 treatment and returned smear positive after at least 8 weeks of interruption of treatment
Transfer in	A TB patient already registered for treatment in one LGA/State who is transferred to another LGA/State where s/he continues treatment.
Other	All cases that do not fit the above definitions. This group includes: • Chronic cases – patients who remains smear positive after completing re-treatment regimen(cat 2) • A patient treated for TB outside the DOTS for more than four weeks and is smear-positive. • A patient diagnose as sputum smear negative TB after a cure or successful treatment • A patient who previously received treatment but outcome of treatment is un-known and now smear positive.

Table 2: Recording treatment outcome in smear-positive TB patients.[28]

Cured	A patient who was smear-positive at diagnosis, who completed 6 or 8 months of treatment and who is smear-negative at the end of 6th or 7th month of treatment and on at least one previous occasion.
Treatment completed	Any patient who was smear-positive at diagnosis and who completed treatment but in whom smear examination results are not available at the end of treatment.
Treatment failure	Any patient who remains or becomes smear positive again at the end of fifth month or later during chemotherapy
Treatment success	the sum of patients cured and those who have completed treatment
Died:	Any patient who dies for any reason during the course of his/her chemotherapy.
Defaulter:	Any patient whose treatment was interrupted for 8 consecutive weeks or more after the date of the last attendance
Transferred out [a]	A patient who has been transferred to another treatment centre in another State and whose treatment result is not known. Note: 'transferred out' is not allowed within the same State; rather the patient can be referred to another LGA and his treatment outcome obtained during the quarterly review meeting

[a] The LGTBLS should obtain the outcome of every patient, including those that were referred to another health facility if possible.

For the purpose of this study, a cohort means a group of TB patient diagnosed and registered for a specified one year period.[44]

RESULTS

Gender and sex distribution of new ss+ PTB in Enugu state, 2005-2009

The modal age group for new ss+ PTB cases in Enugu state was 25-34 years, followed by 35-44 years while 0-14 years contributed the least (Table 3). In general, the total number of male cases registered for the five year period was higher than that of females. Nevertheless, below 15 years of age, the number of female cases was consistently higher than that of males through out the period. For the 15-24 year age group, the sex distribution pattern across the years was not consistent but the total number of female cases was still higher than that of males (Table 3, Fig. 4). For the remaining age groups, males contributed more cases per year than females except in 2009 when the male to female ratio was equal to a unity for the 55-64 year age group. Details of the sex and age distribution of new ss+ PTB cases in Enugu for 2005-2009 are shown in table 3.

Figure 4: Sex and age groups of new ss+ PTB in Enugu state, 2005-2009

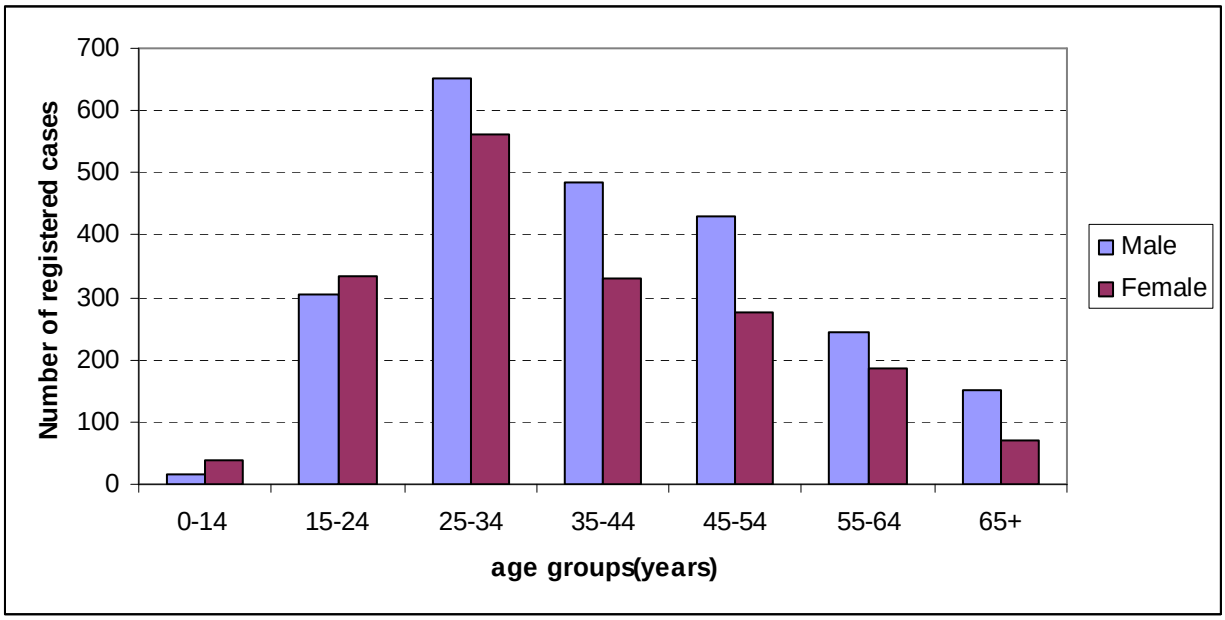


Table 3: Sex and age group distribution of new ss+ TB cases in Enugu state from 2005-2009

Year	Sex (M=male, F=female)	Age group (years)							Sub-total (%)*	Total new ss+ TB
		0-14	15-24	25-34	35-44	45-54	55-64	65+		
2005	M	0	52	131	90	87	43	34	437 (58.7)	745
	F	4	72	104	53	32	31	12	308 (41.3)	
2006	M	0	65	131	83	71	31	29	410 (56.8)	722
	F	8	74	107	65	33	20	5	312 (43.2)	
2007	M	4	62	110	88	78	54	30	426 (57.0)	748
	F	5	58	94	67	55	31	12	322 (43.0)	
2008	M	5	56	151	114	113	58	35	532 (55.1)	965
	F	8	65	141	69	79	46	25	433 (44.9)	
2009	M	8	69	130	109	81	57	24	478 (53.0)	902
	F	13	64	117	77	78	57	18	424 (47.0)	
Total (%)**	All sexes	55 (1.4)	637 (15.6)	1216 (29.8)	815 (20.0)	707 (17.3)	428 (10.5)	224 (5.5)	4082	4082 (100.0)

* – denominator = total new ss+ TB for the corresponding year
** – denominator = sum total of ss+ TB for 2005-2009

Trends of TB case finding in Enugu State, 2000-2009

The reported annual number of all TB cases increased progressively from 914 cases in the year 2000 to 1684 in 2009 except in 2001 and 2004 when it (for each year) was less than that of the preceding year (Table 4). From 2004 to 2009, all cases of TB increased at a mean rate of 7.4% per annum (median 5.2%); the least annual increase of 1.2% occurred from 2004 to 2005 while the highest (16.1%) was reported from 2007 to 2008.

The annual number of new ss+ PTB cases reported over the period was consistently above 500 (Fig. 5). The least (583) and highest (965) number of cases were reported in 2001 and 2008 respectively (Table 4). Unlike the pattern of all TB cases which generally showed a raising trend, except the declines in 2001 and 2004, that of the new ss+ PTB cases appeared to follow an uneven wave-like pattern – one or two consecutive years of increased detection were followed by year(s) of declining detection of new ss+ PTB (Fig. 6). The highest annual increase (29%) for new ss+ PTB was observed from 2007 to 2008. There were increased reports for all TB and smear -ve PTB cases in 2009 while registered new ss+ PTB cases showed a decline (Figs. 5, 6). On the other hand, the proportion of ss+ among the new PTB cases showed a consistent downward trend from 76% in 2005 to 63% in 2009 (Fig. 7). Similar pattern also applied to the proportion of new ss+ of all TB cases (Fig. 7).

After 2004, the number of reported extra-pulmonary TB cases increased markedly (Table 4). The median number of extra-pulmonary TB cases detected over the five year period of 2000-2004 was 36 while that for 2005-2009 was 150, which represents a 4 fold rise.

The annual number of relapsed cases fluctuated across a narrow range of 28-63 over the period with a median of 43 cases (Table 4). Likewise, the median number of treatment failure cases was 8 (range: 4-17). The lowest treatment failure was reported in 2009 while the highest was in 2006.

Table 4: Trends of TB case findings in Enugu state, 2000-2009

Year	New PTB		Other PTB				Extra-pulmonary (%)	All cases	TB/ HIV (%)*
	New ss+ (%)	Smear negative (%)	Relapsed (%)	Failure (%)	Return after default (%)	Others			
2000	626 (68.5)	187 (20.5)	42 (4.6)	16 (1.8)	16 (1.8)	0 (0.0)	27 (3.0)	914	-
2001	583 (67.2)	172 (19.8)	44 (5.1)	9 (1.0)	25 (2.8)	0 (0.0)	34 (3.9)	867	-
2002	675 (62.9)	248 (23.1)	62 (5.8)	7 (0.7)	43 (4.0)	0 (0.0)	38 (3.5)	1073	-
2003	769 (63.5)	285 (23.5)	60 (5.0)	7 (0.6)	45 (3.7)	0 (0.0)	46 (3.8)	1212	-
2004	765 (64.5)	321 (27.0)	28 (2.4)	7 (0.6)	25 (2.1)	0 (0.0)	36 (3.0)	1187	-
2005	745 (62.0)	235 (19.6)	34 (2.8)	11 (0.9)	36 (3.0)	0 (0.0)	126 (10.5)	1201	-
2006	722 (57.6)	289 (23.1)	63 (5.0)	17 (1.4)	57 (4.6)	0 (0.0)	150 (12.0)	1253	-
2007	748 (54.2)	342 (24.8)	52 (3.8)	10 (0.8)	38 (2.8)	13 (0.9)	177 (12.8)	1380	-
2008	965 (60.2)	415 (25.9)	38 (2.4)	5 (0.3)	21 (1.3)	36 (2.3)	122 (7.6)	1602	411 (32.5)
2009	902 (53.6)	515 (30.6)	39 (2.3)	4 (0.2)	16 (1.0)	0 (0.0)	164 (9.8)	1684	414 (36.2)

*The denominator was the total number of all TB cases tested for HIV (1264 in 2008; 1144 in 2009)
- no data available

Figure 5: Trends of PTB detection in Enugu state

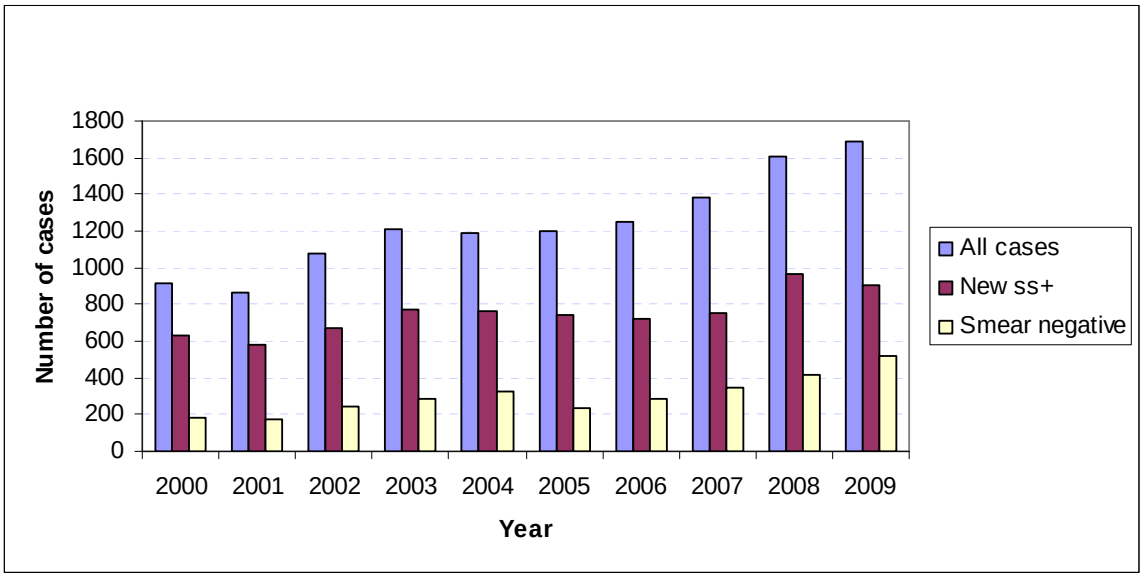


Figure 6: Annual cumulative change in TB case detection in Enugu state

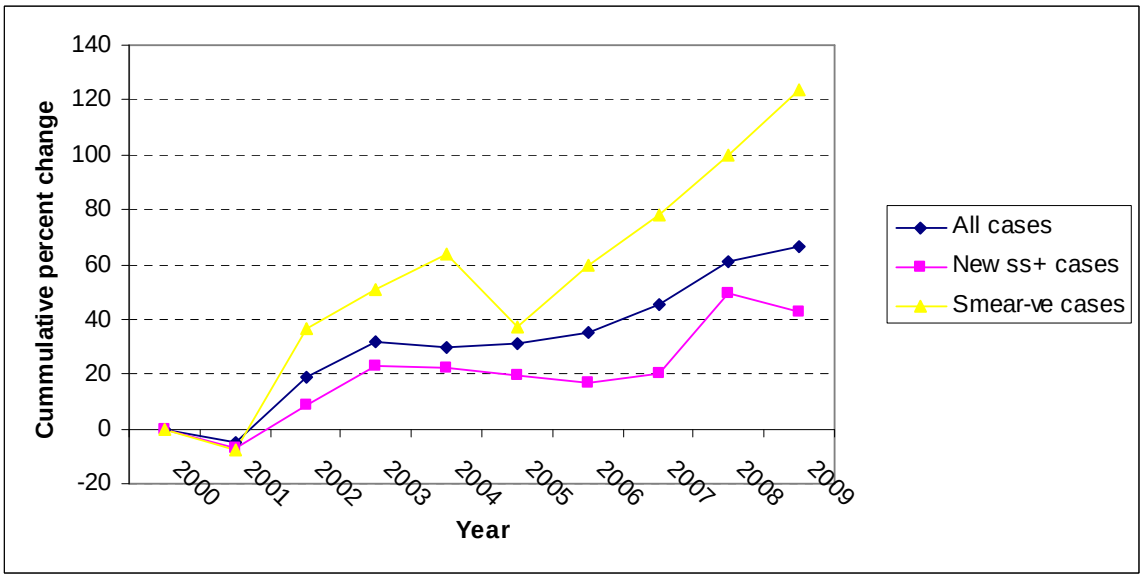
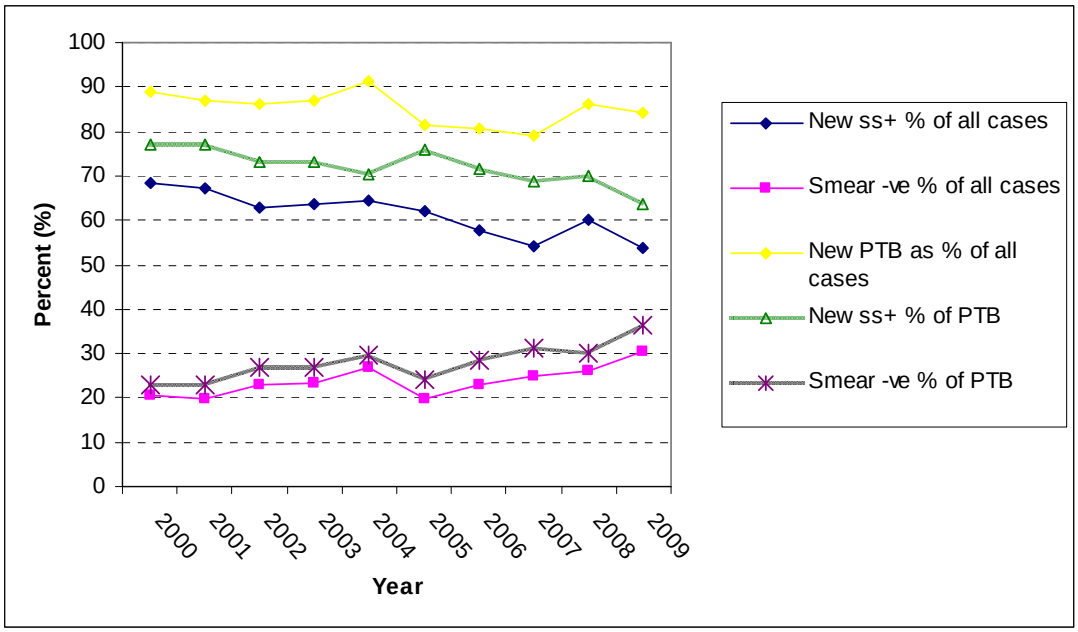


Figure 7: Trends of PTB detection in Enugu state, 2000-2009



TB/HIV co-infection in Enugu state, 2008-2009

The mean prevalence of HIV for all TB cases and new ss+ PTB were 34.4% and 30.7% respectively. Sixty eight percent of all TB cases were screened for HIV in 2009 which was significantly lower than the 79% screened in 2008 [P<0.001, OR = 0.57 (95% CI: 0.48, 0.67)]. A similar significant difference was observed for new ss+ PTB cases (Table 5). Though the prevalence of HIV among all TB cases and new ss+ PTB cases were higher in 2009, the values were not significantly different from those of the preceding year. Details of the available records on HIV screening and co-infection among TB cases in Enugu state are shown in table 5.

Table 5: HIV/TB co-infection in Enugu state, 2008-2009

Parameters	Year 2008 (%)	Year 2009 (%)	p-value	OR (95% CI)
All TB cases tested for HIV	1264 (78.9)[a]	1144 (67.9)[a]	< 0.001	0.57 (0.48-0.67)
New ss+ tested for HIV	848 (87.9)[b]	749 (83.0)[b]	0.003	0.68 (0.52-0.88)
Total HIV+ve all TB cases	411 (32.5)[c]	414 (36.2)[c]	0.059	1.18 (0.99-1.40)
HIV+ve for new ss+ cases	258 (30.4)[d]	232 (31.0)[d]	0.812	1.03 (0.82-1.28)

[a] – denominator = all TB cases reported (table 4)
[b] – denominator = new ss+ cases reported (table 4)
[c] – denominator = all TB cases tested for HIV
[d] – denominator = new ss+ cases tested for HIV

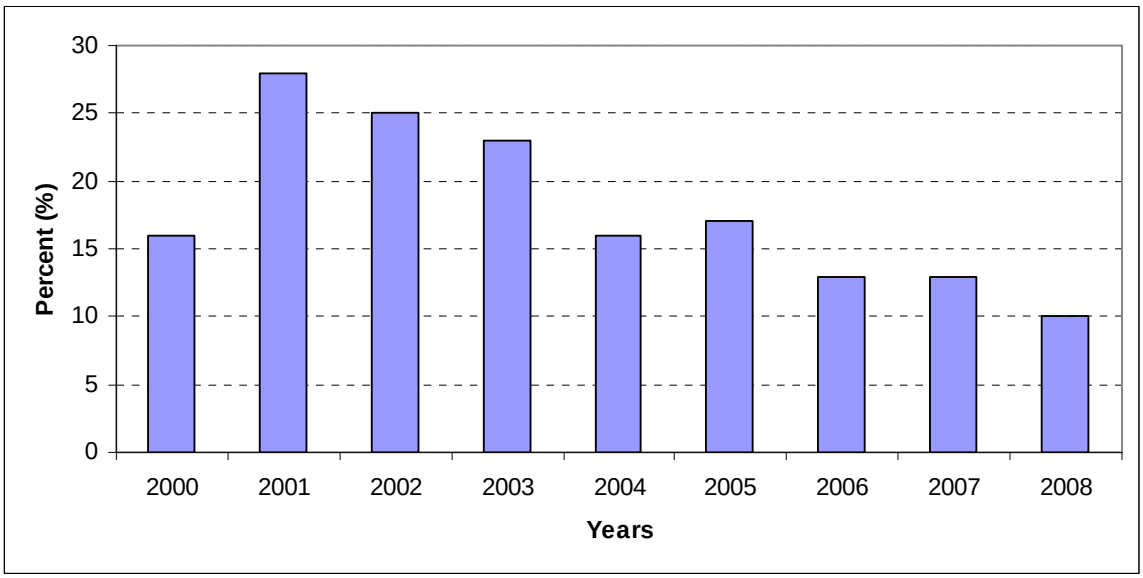
Treatment outcome for new ss+ PTB in Enugu State, 2000-2008

The summary of treatment outcomes (in percent) for the new ss+ PTB cohorts registered at the DOTS centers in Enugu from 2000 to 2008 is shown in table 6. The treatment success rate ranges from 78% in 2006 (and 2007) to 85% in 2001 with a median of 82%. Also, the median cure rate was 65% (range: 57-72). Both treatment success and cure rate showed remarkable increase in 2008 compared to the values of the preceding year. The difference between the treatment success rate and cure rate, which represents treatment completed, showed a near consistent downward trend from 2001 to 2008 (Fig. 8).

Table 6: Treatment outcome (percent) of new ss+ PTB cases in Enugu state

Year	Treatment success %	Cured %	Failure %	Died %	Defaulted %	Transferred out %
2000	84	68	2	5	7	3
2001	85	57	2	4	7	3
2002	83	58	0	6	8	3
2003	83	60	0.6	5	9	3
2004	82	66	1	6	9	1
2005	80	63	0.9	5	12	2
2006	78	65	1	7	10	3
2007	78	65	8	1	9	3
2008	82	72	5	0.8	11	2

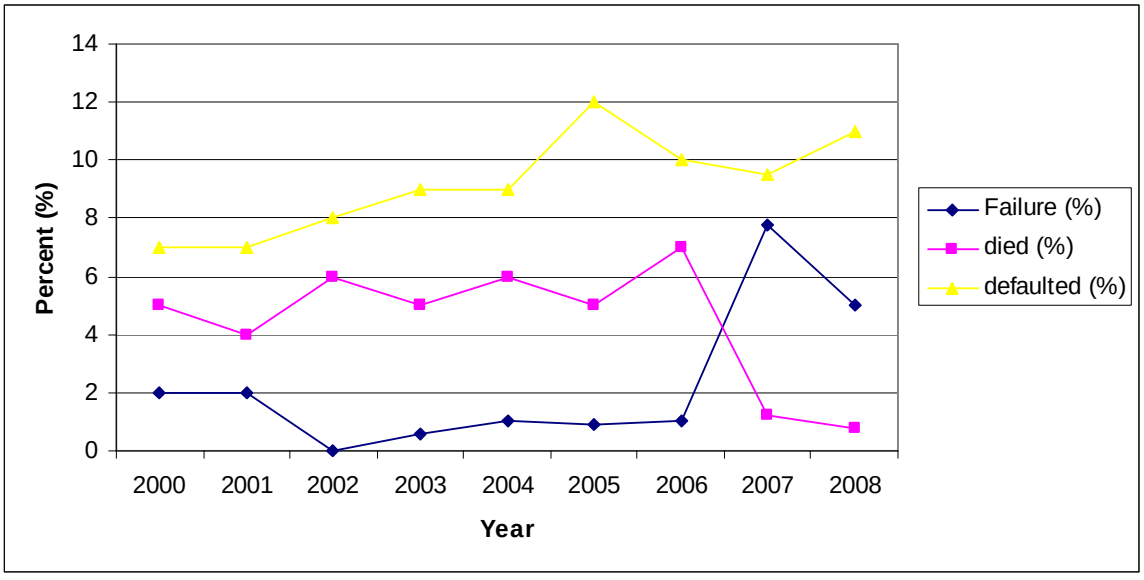
Figures 8: Trend of “Treatment completed” for new ss+ PTB cohorts in Enugu state



The trends of the proportion of new ss+ PTB cases that died, defaulted, or failed treatment are shown in figure 9. Generally, both treatment failure rates and death rates were consistently below 10% of the registered new ss+ PTB cases through out the period. From year 2006 to 2007, the death rates reduced remarkably while the failure rates increased by a similar margin; but in 2008, both parameters declined with varied magnitudes.

On the other hand, the trend of default rates among cohorts of new ss+ PTB cases appeared to be in the upwards direction with occasional declines (Fig. 9). The median default rate was 9% (range 7-12). The highest default rate of 12% was recorded in 2005; incidentally, reduction in both failure and death rates also occurred in the same year.

Fig. 9: Trends of unfavourable treatment outcome for new ss+ PTB cases in Enugu state



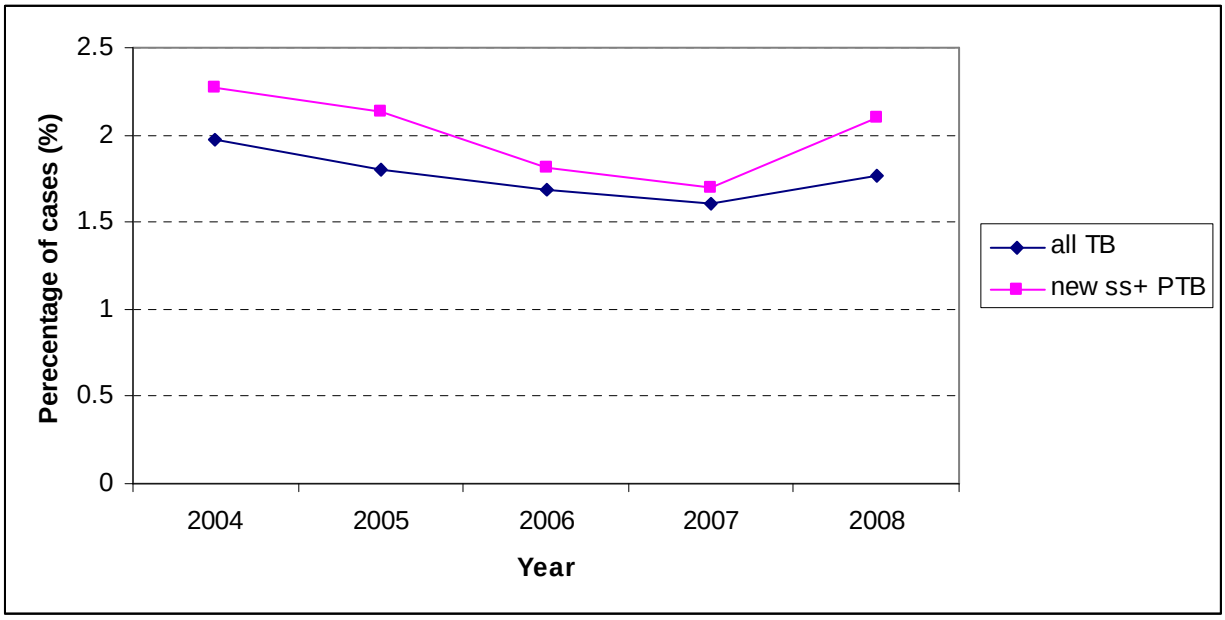
Comparison of the National and Enugu state trends of TB, 2004-2008

From 2004 when DOTS services became nationwide in Nigeria, the percentage of all TB cases reported from Enugu state varied from 1.60% in 2007 to 1.97% in 2004 with a median of 1.77% (Table 7). Likewise, the median percentage of new ss+ PTB cases reported from Enugu state was 2.10%; the lowest value (1.70%) was in 2007 while the highest (2.27%). was in 2004. The percentages of both new ss+ PTB and all TB cases reported from Enugu increased in 2008 despite the progressive decline recorded from 2005 to 2007 (Fig. 10). In all, a TB case reported in Enugu state in 2008, was significantly more likely to be a new ss+ PTB when compared to a national case report [$P < 0.001$, OR = 1.46 (95% CI: 1.32, 1.61)]. Likewise, for the whole period of 2004-2008, a TB case reported in Enugu state was also more likely to be a new ss+ PTB when compared to the whole nation [$P < 0.001$, OR = 1.33 (95% CI: 1.26, 1.40)].

Table 7: Percentages of reported National TB (all and new ss+) from Enugu state

Year	All TB		New ss+ PTB	
	Nigeria	Enugu state	Nigeria	Enugu state
2004	60,290	1,187 (1.97)	33,755	765 (2.27)
2005	66,848	1,201 (1.80)	35,048	745 (2.13)
2006	74,225	1,253 (1.69)	39,903	722 (1.81)
2007	86,241	1,380 (1.60)	44,016	748 (1.70)
2008	90,311	1,602 (1.77)	46,026	965 (2.10)
Total (2004-08)	377,915	6,623 (1.75)	198,748	3945 (1.99)

Figure 10: Percentages of the National TB cases reported from Enugu state



Possible impediments to TB control in Enugu state

The possible impediments to TB control in Enugu state of Nigeria are presented under common themes thus: Community related, Health system related, and Government related impediments.

Community related impediments

Ignorance and health seeking behaviour for TB: Participants (TB cases) in a study from Southern Nigeria,[7] had identified ignorance as the major reason why TB suspects do not report to DOTS centers in the region. With the development of prolonged cough, most people in the community would first seek for care from a drug store and if the symptom persists, other forms of health care would be consulted singly or in combinations. This health seeking pattern was evident in the study where only 1.8% of the respondents presented straight to DOTS clinics without prior care while 48% were first treated at drug stores.[7] It has been found that even among patients diagnosed of TB, some received treatment at drug stores or private health facilities and these forms of care have been shown to contribute majorly to treatment failures and MDR-TB among TB patients.[36]

Also, poor knowledge of the actual cause and transmission of TB may affect the disease control in the State. This may be supported by the report that TB patients who presented within four weeks of symptoms were more likely to know about the aetiology and mode of transmission of the disease unlike those who presented after 12 weeks of symptoms where over 90% were totally unaware of the disease.[45]

Belief and attitude of the community to TB: In Igbo communities generally, it is widely held that TB is caused through witchcraft whereby an enemy poisons the food or drinks of another person. This belief may explain the health care seeking from herbalist and traditional healers after failure of treatment from the drug stores.[7] Health seeking is often determined by people's belief and perception of the disease, treatment experiences, and cost-benefit of the treatment among other considerations.[9;46] The perceived poor attitude of health staff and low rating of the government (public) health facilities,[7;26] within which DOTS is currently delivered in the study area suggest that DOTS centers may only be recommended when other 'friendly' alternative health care fail.

A house-hold survey in South-eastern Nigeria (including Enugu state)[47] showed that TB was ranked lowest among the 10 endemic tropical diseases, in terms of perception of the seriousness of disease occurrence and effects. This finding is unfortunate for TB control in Enugu state because the compliance of a community to any disease eradication programme may not be effective when the disease is viewed as a low-priority health problem.[48]

Other community related factors: There are other factors that may be working against the TB control in the study area. Household over-crowding, which has been identified as an independent predisposing factor for TB control in West Africa,[23] is rampant in Enugu where the house hold size in the community ranges from 8 to 12.[26]

Also, TB has strong association with HIV infection,[2] and the prevalence of the latter in Enugu is the highest in South-eastern Nigeria.[10] This is evident from the first part of this study's results where the available two year data on TB/HIV co-infection showed a HIV prevalence of over 30%.

Health system related impediments

TB treatment by private for-profit health facilities: Communities in Enugu state had scored the government health facilities so low in terms of performance, and majority of the people would rather present to private health facilities when sick.[26] Unfortunately, DOTS services in the State are delivered through the public health facilities because the private public mix (PPM) strategized by the National TB control programme,[20] is yet to evolve in the State. The PPM strategy might have been developed because of the known fact that treatment of TB using orthodox medications was rampant outside DOTS services especially in private hospitals, as well as government hospitals (not supported by national TB programme), and drug stores.[36] TB management in these facilities was found to be grossly inadequate due to the use of un-approved drug regimes, and lack of treatment supervision including direct observation of therapy (DOT).[36] A study of 340 private medical practitioners in Enugu state showed that only 1.5% and 2.6% of them used the recommended anti-TB drug regimes and dosages respectively, while none of them observed the recommended treatment duration for each drug; also, patients' follow-up and mechanism for tracing defaulters were largely non-existent.[49] Another study of private medical practitioners during their annual national meeting noted that 90% of the respondents were involved in TB treatment (new and retreatment cases) but only 20% of this group adhered to the approved guidelines. It is more disturbing to note that 85 and 45 different TB treatment regimens were used by the respondents for new and retreatment cases respectively.[50]

Accessibility of DOTS services: As at 2008, the State had 95 DOTS and 30 microscopy centers,[20] serving the whole 17 local government of the State and over 3 million population spread over 8,727.1 square kilometres. Though the DOTS services are basically free, the obvious inadequate service outlets especially the microscopy centers, raise an accessibility concern because of the possible financial and physical difficulties of accessing the services. The very low number of microscopy centers may have a relationship with the obvious disparity between the treatment success and cure rates observed in the State (Table 6). Though a hospital based study from South-southern Nigeria had identified male sex as the only independent risk factor for TB treatment default,[51] the inaccessibility of DOTS services was not studied and therefore remains a potential impediment.

TB case mismanagement in DOTS centers: Poor history taking and the resultant misclassification of patients' category, drug under-dosing, and lack of DOT were identified in DOTS centers in Southern Nigeria.[36] These had not only contributed to treatment failure and development of MDR-TB but have the potential to erode the fledging community's trust and confidence in the DOTS services thereby encouraging the already favoured alternative treatment options.

The existence of two regimes for the continuation phase treatment of category 1 TB cases, where 6HE is self-administered and 4HR involves DOT,[28] may encourage default from treatment and MDR-TB among the 6HE group.

Government related impediments

Though government financial commitment to TB control in Nigeria has steadily increased over the years, majority of the funding still come from global funds, grants and loans.[6] Nevertheless, a lot of funding gaps still exists within DOTS mainly the laboratory supplies and equipment,[6] and the government at all levels should work towards filling the

gaps. The 2008 annual TB report of Nigeria subtly noted an effect of inadequate funding on the Enugu state TB control programme thus "… the state TB/HIV working group was able to identify gaps that exist in the TB & Leprosy program , the shortage of funds have however hindered the sittings of the committee."[20]

Finally, it was recently observed that TB drug warehousing activities in Nigeria did not reflect the good warehouse practice and this sub-optimal performance has the potential of severely compromising TB supplies if they recommendation of the study group were not implemented.[52] The stock out of anti-TB drugs which was noted 2007 in Nigeria,[6] might have been related to the poor warehouse practices.

DISCUSSION

Trend of TB in Enugu state of Nigeria

The sex and age patterns of new ss+ PTB found in this study are consistent with the known epidemiology of the disease.[6;45;53] The age distribution in the study is very similar to the national report of 2008 with 25-34 years as the modal age group. The study's findings are in line with the belief that TB is a disease of adults and that the burden of the disease lies more with the male sex.[53] Male to female ratio among new ss+ PTB cases may be associated with the HIV prevalence in the general population and it has been shown that more female than male cases of TB are detected in countries with HIV prevalence of above 1%.[6] Nevertheless, considering the HIV prevalence in the study area, it is obvious that Enugu State of Nigeria is a deviation from that general assertion. Furthermore, the TB burden in the State was consistently higher in females than males for 0-14 year age group (male/female < 1). This sex pattern within that age group was not obvious in the national report[20] but, it is consistent with the current global pattern of the disease.[6] Currently, there are no clear explanations for the higher notification of TB in males than females;[6] the confusion must have been compounded by the observed female TB case preponderance within the 0-14 year age group.

The number of all TB cases reported annually in Enugu state showed a raising trend but the proportion of new ss+ PTB cases has been declining (Fig. 7). Though these trends were also observed in the national report,[20;42] it should however stimulate further research especially as regards the quality of the microscopic centers within the DOTS services of the State and Nigeria. The prevalence of HIV infection among TB cases in this study was over 30% (Table 5); therefore HIV/TB co-infection can also explain the declining proportion of new ss+ PTB because TB patients who are HIV- positive are more likely to be sputum smear negative.[2]

The 4-fold increase in the detection of extra-pulmonary TB cases which started in 2005 is very remarkable. It is unlikely that the prevalence of this category of TB increased in the State rather, the notification might have been emphasized from that year by the TB programme – key informant interview of State programme officers would have helped to clarify this assumption.

The proportion of registered TB patients that were failure or relapse cases declined from 2006 (Table 4). This trend may suggest an improved TB management at the DOTS centres which may be consistent with the reported TB programme's operational changes that followed the MDR-TB study in Enugu.[36] These operational changes include the creation of awareness among national TB programme personnel on the mechanism of TB drug resistance and its prevention, the introduction of "dosage-friendly" FDC anti-TB packs, addition of the regimens 2RHEZ/4RH for category I treatment.[36] However, it is equally likely that the number of the patients registered, did not represent the true picture of these categories of patients in the community. Noting that health seeking behaviour is related to treatment experience by patients and community among other determinants, it is likely that patients who relapsed or failed treatment may loose confidence in the DOTS services and seek alternative care from other sectors.

Records of HIV/TB co-infection within the Enugu state TB programme apparently started in 2008 as suggested by the available data (Table 5). The percentage of all TB cases that tested positive to HIV was 32.5% and 36.2% for 2008 and 2009 respectively. Despite the possible effect of non-response (those not screened) which was higher in 2009, the figures should be considered as high. It is far higher than 27% which was the WHO estimate for Nigeria in 2007 and the 26.8% reported from a DOTS/GLRA supported community hospital from a neighbouring Imo state.[6;45] Just like the HIV prevalence in the general population, available data (unpublished) showed that the prevalence of HIV among TB

cases in Enugu state was also the highest in South-eastern Nigeria However, another serious concern is that the proportion of TB cases (all cases and new ss+) tested for HIV reduced significantly in 2009 when compared to the preceding year (Table 5). Likewise, over 30% of all TB cases registered in 2009 were not screened for HIV despite the proven association and the need to initiate anti-retroviral management for co-infected patients.[28] Considering the high prevalence of HIV among those TB cases screened, the likely scenario is that about 30% of those not screened would be HIV-positive which implies that their TB treatment were not holistic since they did not benefit from anti-retroviral treatment. The high proportion of TB cases that were not screened for HIV, calls to question the quality of HIV counselling and testing (HCT) offered to TB patients in the State. However, if we assume an optimal HCT then, there may be the need for a change of counselling and testing strategy because it has been shown that refusal of certain option of HCT is not unusual among TB patients.[54;55] The best strategy will be the "diagnostic HIV testing" which implies routine testing of all TB cases as recommended by the WHO.[56] However, to address the issue of patients' consent, the "Provider initiated HIV counselling and testing (PIHCT) with opt-out option",[56;57] which is currently used in antenatal services in Nigeria, will also be a more effective alternative to the "opt-in" option practised by State TB control programme.[28] In the "opt-out" option, every TB patient receives pre-test information followed by HIV testing which s/he is free to reject but in "opt-in", after the pre-test information, the patient must express consent before HIV testing is provided. It is believed that the introduction of the "opt-out" option to disease screening programme in Nigeria will provide the required "prompting" necessary to overcome the inertia and fear that may delay or prevent the screening of at-risk individuals.[58;59]

Treatment outcomes of TB in Enugu state

Though the State's median treatment success rate of 82% falls short of the national target of 85%, it is still higher than the national value of 78%,[6] which suggests good performance by the States TB programme. However, treatment success rate for years 2000-2003 were consistently higher than those of 2004-2008 and similar picture was also observed with the treatment default rate (Table 6) which may imply a reduction in patients' compliance in the recent years. The reasons for the disparity should be explored by the State TB programme so as to improve the disease control. On the other hand, the disparity between treatment success rate and the cure rate may suggest inadequate laboratory support which appeared to have improved in 2008 when the lowest disparity (10%) was recorded. It is recommended that 1 microscopy center should serve 100,000 population.[6] Assuming that the State's 2006 census figure of 3,257,298 million and the 2010 estimate of 3,564,679 were correct, then Enugu state should have at least 37 microscopy centers. However, it is widely held that that the 2006 census figure for the South-eastern zone of Nigeria was a gross and deliberate under-representation of the true population of the Igbo speaking States for several reasons including the attempt to reduce the significance of their agitation for equitable distribution of the number of States among the zones of the country by creation of more States from South-eastern zone. It is therefore very likely that the true population of Enugu state is far higher than the current estimates and would require a lot more microscopy centers.

Treatment of TB in Nigeria is standardized for each patient category. Therefore, since under dosing and risk of monotherapy must have been minimized by the introduction of FDC drugs, it is possible that misclassification of category 2 patients as category 1 in the DOTS services as noted in Southern Nigeria,[36] may be the major contributing factor to treatment failures in Enugu state. It takes repeated sputum microscopy at specified

treatment interval (annex 1) to declare a TB case as a treatment failure and during this "waiting period", s/he is a risk to the community. Therefore, proper patient categorization should be viewed as important as quality control of microscopy centers and a mechanism for the routine monitoring of the performance of TB health staff should be developed and enforced.

Impediments to TB control in Enugu state

Ignorance has been identified as the major reason why TB suspects in Southern Nigeria do not present to DOTS centers.[7] Though the referred study did not define the direction of ignorance but it could be derived from the context of the study's discussion that it meant the ignorance as regards the existence of, and treatment capability of DOTS centers. This assumption is based on the fact that TB is not alien to the Igbo population of Nigeria and the disease is described by various names in different dialects of igbo language e-g. "ukwara nta"; however, the general belief about the disease's aetiology, transmission and treatment differ from those of the biomedicals. This fact may be supported by a study from a neighbouring South-eastern state (Abia state), conducted among respondents randomly selected from bus terminals and markets, which showed high levels of knowledge of TB (including its clinical signs) that was not affected by respondents' age groups, sex, occupation and educational level.[60] It is argued that the poor spread of DOTS centers and the delivery of its services through public health facilities, which are poorly perceived and utilized by the communities in the State, might have contributed to the existing ignorance of the DOTS services. A well monitored community TB control programme guided by research based knowledge of the beliefs and attitude of the community, with full community participation in the programme planning and execution may help to decentralize TB control measures beyond the health facilities, improve case detection, reduce patient stigma, and increase access to effective TB care.[46] It may also

help to change the belief and attitude of the people toward TB aetiology and treatment which will further reduce TB care seeking from drug stores and herbalists. Likewise, retraining of the private medical practitioners in Enugu state and their full and monitored involvement in TB patients' care will enhance TB notification and care in the State. The community TB control programme and PPM strategies were recognized by the recent report and manual of the National TB programme but their implementation may still be evolving. A report from Kaduna state of Nigeria where PPM has been introduced by the State's TB programme, has confirmed the effectiveness of the strategy - the average number of TB cases registered by each private health facility was approximately twice that of a public facility, and the treatment success rate of the private facilities was also higher that the public facility.[61]

The WHO report showed that as at 2007, Nigeria TB programme used 6HE for continuation phase treatment of category 1 TB cases which suggests that the two drug regimens (6HE and 4HR) stated in the national manual were introduced in 2008. Nevertheless, the effect of the addition of the new regime (6HR) is not obvious if the annual proportion of treatment failure is used as an indicator of effective treatment (Table 6). The probable explanation could still be patients' misclassification as well as the non-supervision (DOT) of those receiving the 6HE regime. By the introduction of such a guideline by the National TB programme may unknowingly be encouraging non-supervision of anti-TB drug administration, contrary to the DOTS guideline.

Finally, the need for improved government financial commitment to TB programme cannot be over-emphasized. Assuming that resources available to the TB programme are allocated properly and managed transparently, the report that the Enugu state TB working committees could not meet to discuss identified gaps, was a pointer to the real financial state of the State's TB Programme. It is obvious that the TB programme in the Enugu

state and the whole Nigeria is driven with donor funds therefore, programme sustainability in future without the global funds remains a big concern.

Study limitations

This study is limited by the use of "cleaned" secondary data from the State's TB programme and the researcher did not partake in data cleaning and the associated considerations. Errors could have occurred during data entry and computations, by the State TB programme, but were likely to be very minimal and would not have affected the results of the study. However, authenticity of the data is not in doubt because the State TB programme receives technical assistance from the WHO zonal office in the State.

Most importantly, the disease trends identified in the study only represent cases managed in DOTS centers which cannot be the true situation in a population where a lot of treatment options exist. The assumption is in line with United Nation's opinion that the TB data reported by ministries in developing countries were usually only a fraction of the real population figures.[3] Also, due to incomplete data, the period of years reviewed for all study objectives was not uniform and had limited trend assessments for some variables such as HIV/TB co-infection.

Furthermore, the possible impediments identified in the State's TB programme were based on deductions from literatures originating form the State and similar environments therefore, publication bias and over-generalization from small sized studies could have limited the study findings. It is also recognized that the barriers identified in the study could not have been exhaustive and may have under-estimated or over-estimated the magnitude and extents of the problems.

Nevertheless, since the study is essentially the first formal effort at articulating and publishing the TB burden and control barriers in the State, it is hoped that the study will stimulate and direct policy relevant researches in the subject area.

CONCLUSIONS

Conclusions

The study has demonstrated an increasing trend of TB cases in Enugu state of Nigeria for the 10 year period of 2000-20009. All TB cases and new smear negative PTB showed a near consistent raising trend, while that of the new ss+ PTB was fluctuating. The annual number of extra-pulmonary TB which increased by 4-folds in 2005 and persisted afterwards could be a reporting bias. Also, HIV prevalence among TB cases in Enugu state is high just like in the general population.

Furthermore, the contribution of Enugu state to the TB burden of Nigeria is low and the new ss+ PTB treatment success rate in the State is slightly below the set target. On the average, the States contributes 1.77% of all TB cases and 2.10% of new ss+ PTB to the national annual TB register; however, a TB case registered in the State is more likely to be new ss+ PTB when compared to the whole nation.

Finally, the possible threats to the effective TB control programme in the State include ignorance of the residents about DOTS services, lack of confidence in the public health care delivery system through which DOTS operates, misclassification of patients' category within the DOTS system, non-compliance of private medical practitioners to the approved TB treatment guidelines, and inadequate funding.

Recommendations

In addition to the few recommendations made within the study discussion, the following recommendations derived from the study will enhance TB control in Enugu state of Nigeria.

- The State's TB programme should adopt the PPM which has been shown to be effective in Kaduna state of Nigeria. This partnership should start with the retraining of the private medical practitioners on the current TB management. The

researcher will facilitate the use of the existing quarterly continuing medical education (CME) programme for medical practitioners organised by the Enugu state chapter of the Nigerian Medical Association (NMA), as a medium of the retraining.

- The national treatment guideline which also guides the State's TB programme should be revised in line with the current WHO guideline.[5] Most importantly, the use of 6HE for the continuation phase of category 1 cases should be discontinued. Also the "blind" commencement of re-treatment without DST should be minimized by developing more DST centers. These will maintained the presumed low MDR-TB in the country.
- Intermittent retraining of health staff in the DOTS services on the skills of history taking from TB suspects so as to avoid misclassification of patients' categories. A mechanism for monitoring staff performance, in this respect, should be developed and enforced.
- Guideline for PTB diagnosis (Fig. 1) should be revised in line with the current WHO definition of new sputum smear-positive PTB because of the benefits already discussed. Likewise, the entry point for TB screening of cough for 2 or more weeks (Fig. 1) should not be applied rigidly considering the known problem of recall and the emerging evidence that duration of cough does not affect diagnoses of TB.[25] Holistic review of patients' history and clinical signs should be used to triage those with lower duration of cough
- More DOTS centers and microscopy centers should be developed in the State. However, quality assessment (especially external) should be stepped up for the microscopy centers. This will ensure that poor laboratory quality is not contributing to the observed reduction in the proportion new ss+ PTB.

- Though, information alone may not guarantee change of belief and attitude but, it is needed before any change can occur.[62] Therefore, information about the growing burden of the disease in the State as documented in this study should be fed back to the communities in the State through the existing administrative structures such as women meetings, and religious meetings.
- Guided by research based knowledge of the beliefs and attitudes of the communities towards TB, the State's TB programme should stimulate partnership with the communities in adapting and implementing the national community TB guideline. This will ensure that every TB suspect within a community is identified and properly treated.
- Most drug store are registered under pharmacists therefore, the State's TB programme should work through the Pharmaceutical Society of Nigeria to discourage treatment of chronic cough at the drug stores by educating them on the availability and effectiveness of DOTS centers in the State
- Health education in primary and secondary schools should be re-energized and used to disseminate information about TB burden, transmission and the available treatment sites to the households
- The State TB programme should improve on its record keeping and data storage. Use of effective and updated anti-virus for its computers should be encouraged
- In the face of serious financial difficulties, very important committee meetings of the State's TB programme could be financed by indigenous organization and charity bodies if adequately mobilized.

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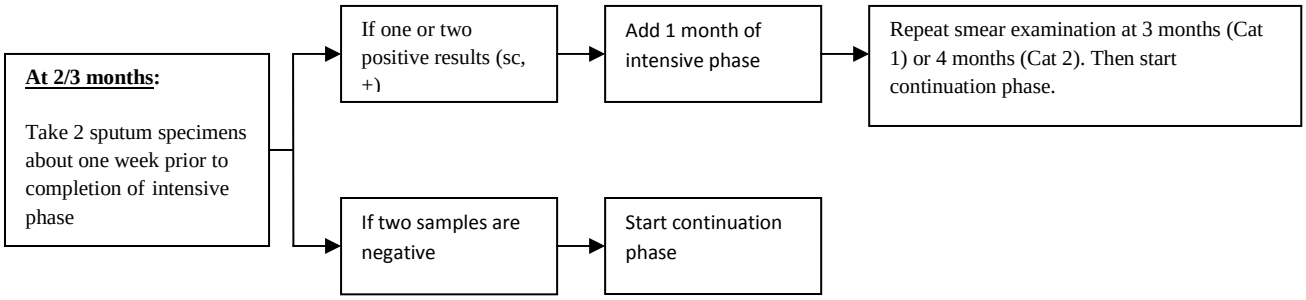
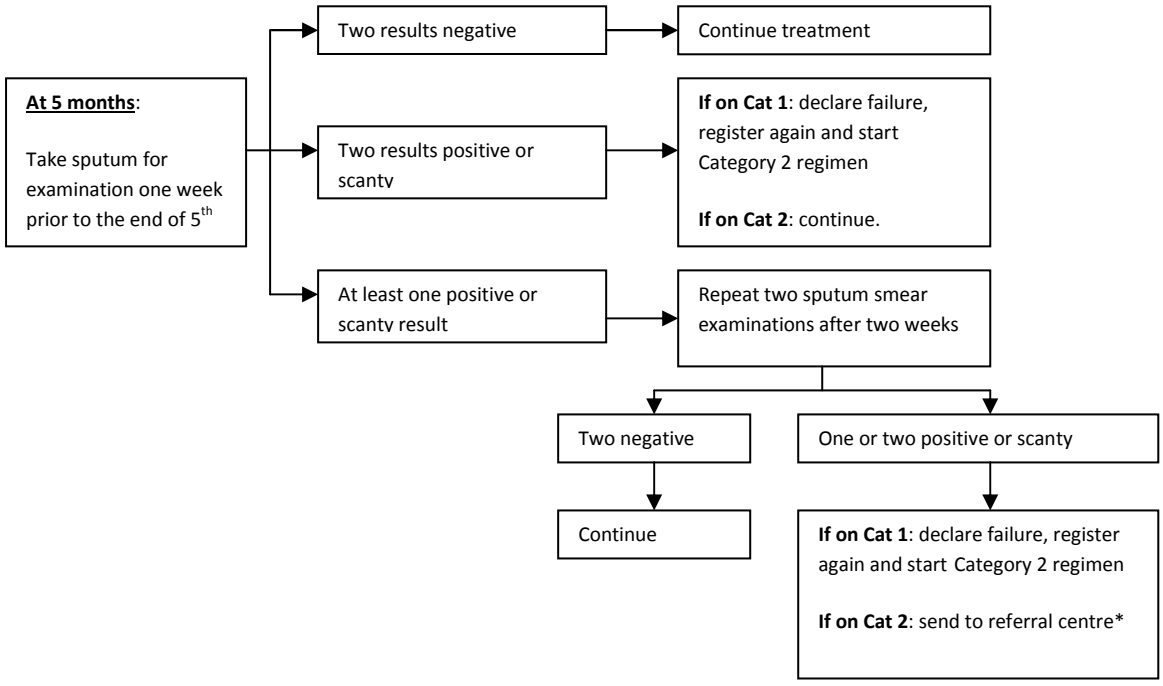
ANNEXES

Annex 1: Follow up of PTB patients in Nigeria using sputum smear microscopy[28]

A: Intensive treatment phase



B: Continuation treatment phase (5th month)



C: Continuation treatment phase (6/7th month)