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Pulmonary tuberculosis in Ibadan: a ten-year review of laboratory reports (1996-2005)

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Summary
Tuberculosis (TB) control programme is a balance between accurate diagnosis of the disease and effective treatment of cases to eliminate the disease in the community. We carried out a retrospective review of the specimens processed in the TB laboratory of the Department of Medical Microbiology, University College Hospital, Ibadan between 1996 and 2005. Majority of the specimens processed were sputum (75.2%) while cerebrospinal fluid and aspirates from other sources accounted for 4.3% and 20.5% respectively. Of the sputum processed, 2,738 (62.4%) were from male patients while 1,650 (37.6%) were from female patients giving a male to female ratio of 1.66:1.00. Only 380 (9.5%) were reported smear positive while 477 (10.9%) were positive for culture. Three hundred and four (6.9%) were smear negative but culture positive while 207 (4.7%) were smear positive but negative for culture. Those sputum that were missed by smear microscopy (6.9%) were only confirmed by culture after six to eight weeks incubation. This culture method is only available in few reference centers in Nigeria. Thus, undiagnosed cases resulting from inadequate diagnostic facilities contribute an impediment to TB control efforts in the community. Hence there is an urgent need to have more accurate, affordable tools that would be available for use at the all levels of health care to achieve total eradication of TB in the community.

Keywords: *Tuberculosis, diagnostic tools, smear microscopy, culture method*

Résumé
Le programme de contrôle de la tuberculose (TB) est une balance entre le diagnosie précis et le traitement adéquate des cas afin d'éliminer cette maladie dans la communauté. Nous avons effectués cette revue rétrospective des échantillons des gouttes épaisses au laboratoire de Tuberculose, Département de microbiologie du Collège Universitaire Hospitalier (UCH) Ibadan entre 1996 à 2005. La majorité des échantillons étaient les échantillons du crachat (75.2%) ; alors que le fluide cérébrospinale et fluide aspiré d'autres sources estimaient à 4.3% et 20.5% respectivement. 62.4%(2,738) des crachat analysés étaient des males et 37.6%(1,650) des patients femelles, ayant une proportion de 1.66 : 1.00. Seulement 380 (9.5%) étaient rapportés positive et 477(10.9%) positive par culture. 304(6.9%) avaient des gouttes épaisses négative mais positive par culture et 207 (4.7%) avaient des gouttes épaisses positive mais négative par culture. Les crachats donc les lames des gouttes épaisses étaient perdu (6.7%) pour la microscopie étaient confirmées par culture ares 6-8 semaines d'incubation. La culture n'est disponible que dans quelques centres des soins de santé de référence au Nigeria, ainsi les cas inadéquatement diagnostiqués restent un problème aux efforts de contrôle de la tuberculose dans les communautés. Nous recommandons un besoin urgent des instruments précis, non-couteux dans les centres de soins de santé afin d'assurer une éradication totale de cette maladie.

Introduction

It was estimated some years back that up to 43% of the world's population was infected with *Mycobacterium tuberculosis* [1], the causative agent of tuberculosis (TB). It is now known that the global burden of TB is increasing especially in developing countries of Africa and Asia where about two-thirds of the cases reside [2,3] With nine million cases and two million deaths each year [4], TB epidemic is regarded as one of the most important global challenges facing man.

Tuberculosis has been with us for too long, for this reason World Health Organization (WHO) declared the disease a global emergency in 1993 also, 46 member states of the Africa Union (AU) declared it a regional emergency in August 2005 [4]. The disease TB continues to be found where there is poverty, in people living in overcrowded and unsanitary environments and where health is already under siege from malnutrition, co-infection with HIV and other debilitating conditions.

Accurate laboratory diagnosis of TB remains the cornerstone of eradicating the disease worldwide [3]. In spite of the huge public health burden ascribed to TB, its diagnosis still relies on old and imperfect technologies for example, WHO acclaimed tool for TB diagnosis (smear microscopy) was invented a century ago. Smear microscopy as a diagnostic tool is unsuitable for paediatric, extra-pulmonary and latent infections. More importantly, it performs poorly in TB/HIV co-infections. The impact of this scenario is mostly felt in disease burden countries of sub-Saharan Africa where TB epidemic is largely driven by HIV scourge.

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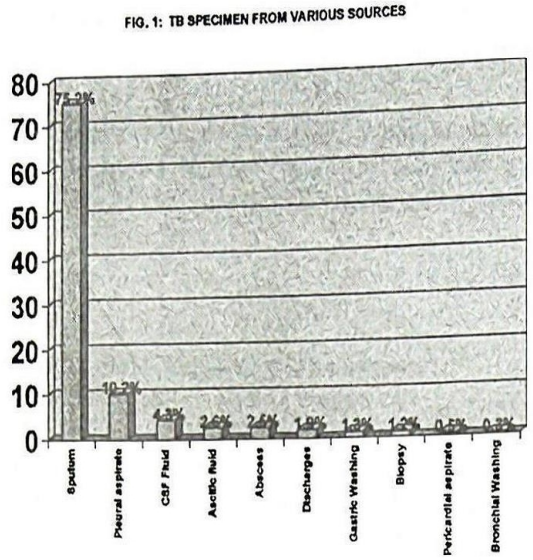

Fig. 1: TB specimen from various sources

There is paucity of data on laboratory diagnosis of TB in Nigeria hence this study was set out to obtain information on current TB diagnostic tools in a reference tertiary centre. This information would be useful for planning strategies for TB control programme in this environment.

Materials and method

This ten-year laboratory based retrospective study (1ST January 1996- 31ST December 2005) was carried out at TB laboratory of the Department of Medical Microbiology and Parasitology, University College Hospital (UCH), Ibadan, Nigeria. TB laboratory in UCH, Ibadan is one of the earliest designated laboratories for diagnosis of TB in Oyo State by National TB and Leprosy Control Programme. It is the only laboratory with facilities for TB culture in the state. Specimens are received from the hospital patients and also from other adjoining health care facilities. Information of all specimens that were sent to TB laboratory was retrieved from the available laboratory records. Results of the sputum smear microscopy and culture were sought out and collated on a yearly basis.

Three sputum specimens from each patient were collected onto wide-mouth container covered with lid. They were then transported to laboratory for processing. Specimens containing saliva were discarded. Each smear was stained by using Ziehl-Neelson (ZN) reagents and then cultured onto Lowestein-Jenson (LJ) medium, incubated at 37°C for six-eight weeks. Suspicious isolates on LJ medium were confirmed by re-staining with Z-N reagents at two, four, six and eight weeks of incubation.

Susceptibility testing and genetic profile of the isolates were not done due to lack of facilities. Information such as age and sex of patients who submitted sputum were also obtained from the available register.

Data Analysis

The data collected were analyzed with the aid of the Statistical Package for Social Sciences (Windows Version 10.0 Chicago, United States) computer software. Data exploration was carried out by examining the frequency of distribution of all the variables obtained from the laboratory register. Presentation of results was done by using tables and charts. Laboratory variables and demographic characteristics of patients who submitted sputum were described in form of proportions and percentages.

Results

Five thousand, eight hundred and thirty two specimens were processed during the ten-year period. The majority (75.2%) were sputum samples while cerebrospinal fluid and aspirates from other sources accounted for 4.3% and 20.5% respectively (Fig 1).

Table 1: Number of sputum specimen processed according to year between 1996-2005

Year	Number	Percentage
1996	588	13.4
1997	487	11.1
1998	379	8.6
1999	512	11.7
2000	644	14.7
2001	-	-
2002	62	1.4
2003	420	9.6
2004	616	14.0
2005	680	15.5
Total	4388	100

Of the 4,388 sputum submitted for analysis, 680 (15.5%) were received in 2005, 616 (14.0%) handled in 2004 while no specimen was processed in 2001 but only 62 (1.4%) were processed for smear microscopy in 2002 (Table1). Out of the total sputum processed, 2,738 (62.4%) were from males and 1,650 (37.6%) from females, giving a male to female ratio of 1.66:1.00. The ages of the patients who submitted sputum were between 10-79 years. Table 2 shows the age and sex distribution of patients who submitted sputum during the study period.

Table 2: Age and sex distribution of subjects who submitted sputum samples

Age group (Years)	No of Patients Male	Female	Total
10-19	87	181	268 (6.1)*
20-29	326	276	602 (13.7)
30-39	423	315	738 (16.8)
40-49	711	78	789 (18.0)
50-59	534	528	1062 (24.2)
60-69	554	106	660 (15.1)
70-79	103	166	269 (6.1)
Total	2738	1650	4388 (100)

**Numbers in parenthesis are in percentages*

Three hundred and eighty (9.5%) were reported smear positive while 477 (10.9%) were positive for culture (Table 3). Furthermore, 304 (6.9%) were smear negative but culture positive while 207 (4.7%) were smear positive but negative for culture. The majority, 3704 (84.6%) were smear and culture negative while only 173 (3.9%) were positive for both smear and culture (Figure2).

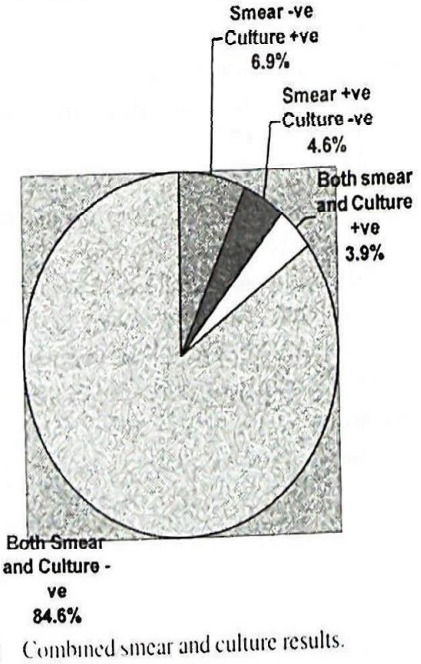

Fig. 2: Combined smear and culture results.

Table 3: Smear and culture results

Result	Smear microscopy	Culture
Positive	380 (8.7%)	477 (10.9%)
Negative	4008 (91.3%)	3911 (89.1%)
Total	4388 (100)	4388 (100)

Discussion

It has been suggested that more attention should be paid to accurate laboratory diagnosis of TB, especially now that TB upsurge is being driven by HIV/AIDS scourge, widespread poverty and weakened health systems in sub-Saharan Africa [5].

This study shows that sputum constitutes the majority (75.2%) of the specimens submitted for analysis. This is not surprising since the commonest presentation of TB is pulmonary. This is not to say that extra-pulmonary TB (EPTB) are not common. Ige *et al* [6] reported 22.4% prevalence of EPTB cases in the same center in 2005 while a study in Ile-Ife documented 12.3% prevalence [7]. Similarly, 18.5% of the population studied in a Tanzanian hospital by Richer *et al* [8] had EPTB. Relatively low percentage of specimens required for diagnosis of EPTB in this study may be due to difficulty in obtaining such samples.

We observed that no sputum was processed in 2001 and only 62 (1.4%) in 2002. The closure of the laboratory between January 2001 to September 2002 accounts for the low patronage. The laboratory was closed down by the hospital management to effect some repairs on the structural defects in order to guarantee the safety of workers.

A slightly higher percentage of sputum (15.5%) was processed in 2005. This is due to the fact that towards the end of 2005, our laboratory started receiving specimens from Anti-Retroviral Clinic (ARV clinic). This clinic is a designated clinic for the treatment and management of patients with HIV/AIDS in UCH, Ibadan. TB has been reported as one of the commonest presentations of HIV/AIDS not only in Nigeria but also in other parts of sub-Saharan Africa [9]. The two disease entities constitute a formidable public health burden in this part of the world where resources and logistics to curtail the scourge is inadequate.

About half of the specimen processed (48.5%) were from patients within the age bracket 20-49 years. This agrees with previous studies [6,7,10] and confirms the high annual risk of infection with *Mycobacterium tuberculosis* in patients below 50 years. This age bracket corresponds to the economic vibrant age of the population which implies that TB constitutes a strong economic burden which could cripple the work force of the population.

Majority (91.3%) of the specimen processed were smear negative. Smear microscopy is the only widely used diagnostic tool in most developing countries with high

burden of TB. Smear microscopy has a low sensitivity as its' major drawback [4]. This low sensitivity may drop from 40% as seen in field settings to 20% in HIV co-infection [4]. Thus some patients may be left undiagnosed leading to delay in initiating therapy and this favors transmission of the disease in the community.

Only 477 (10.7%) were culture positive. Isolation of the causative organism on culture media remains the only definitive criteria for laboratory diagnosis of TB [9]. Culture on LJ medium requires six to eight weeks incubation. The resulting diagnostic delay favors wide transmission of the disease in the environment hence new culture methods that would obviate diagnostic delay are urgently needed for prompt initiation of therapy and to curb the transmission of the disease. Newer culture methods such as TK medium (Salubrics InC, USA) [11] and BD MGIT ™ (Mycobacterium Growth Indicator Tube System, Becton Dickson & Co, USA) [12] are being proposed to replace conventional LJ medium in developing countries. TK medium shortens incubation time to three to four weeks and also allows routine drug susceptibility testing while BD MGIT ™ provides results within 10-14 days. There is need to assess the suitability of these new diagnostic methods in our environment.

Furthermore, 304 (6.9%) of the sputum processed were smear negative but culture positive. Patients with this kind of results are referred to as acid-fast bacilli (AFB) smear-negative pulmonary TB patients. High incidence of AFB smear-negative results is often associated with TB/HIV co-infections [2]. Patients with co-infection tend to produce less AFB in their sputum. This scenario overloads the laboratory and erodes the predictive value of microscopy thus constituting a serious threat to TB control efforts. Those who were smear positive but culture negative (4.6%) may be due to low specificity of smear microscopy, which fails to differentiate pathogenic strains from commensals.

In conclusion, an urgent need exists to adopt more rapid and accurate TB diagnostic tests to shorten diagnostic delay often associated with culture method and low sensitivity and low specificity associated with smear microscopy not only in Nigeria but also in other disease endemic countries of sub-Saharan Africa.

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References

1. American Thoracic Society, Diagnostic Standards and Classifications of Tuberculosis in adults and children. Am J Respr Crit Care Med 2000; 161: 1376-1395.
2. Corbett EL, Watt CJ Walker N *et al.* The growing burden of tuberculosis: Global trends and interactions with the HIV epidemiology. Arch Intern Med 2003, 12; 163: 1009-1021.
3. WHO. Global Tuberculosis Control. World Health Organization Report, 2000; Geneva: WHO/CDS/TB/2000.
4. WHO. Global Plan to STOP TB (2006-2015): Actions for Life: Towards a world free of Tuberculosis. Geneva: World Health Organization 2006; 24-140.
5. WHO. Addressing Poverty In TB Control: Options for National TB Control Programmes. Geneva: World Health Organization 2005; 10-31.
6. Ige OM, Sogaolu OM, Ogunlade OA. Pattern of presentation of tuberculosis and the hospital prevalence of tuberculosis and HIV co-infection in University College Hospital, Ibadan: A review of five years (1998-2002). Afr J Med and Med Sci 2005, 34; 329-333.
7. Erhabor GE, Adebayo RA, Omodara JA *et al.* Ten review of pattern of presentation and outcome of pulmonary tuberculosis in OAUTHC, Ile-Ife. Nig J of Health sciences 2003, 3: 34-37.
8. Richer C, Ndosi B, Mwanmmy AS, Mbwanbo RK. Extra-pulmonary Tuberculosis- A simple diagnosis? Trop Geogr Med 1991; 43: 375-378.
9. Grange JM and Zuma A. The global emergency of Tuberculosis: what is the cause? Journal of the Royal Society for the Promotion of Health 2002; 122: 78-81.
10. Sutherland I. Recent studies in the epidemiology of tuberculosis based on the risk of being infected with tuberculosis bacilli. Advances in Tuberculosis Research 1976; 19: 1-63.
11. www.salubrics.com. Foundation for Innovative New Diagnostics (FIND) to invest into TB test that will cut culture time to half, July 2004.
12. www.bd.com. Foundation for Innovative Diagnostics (FIND) and Becton and Dickson InC. (BD InC.) combine international efforts to improve rapid TB diagnosis for HIV positive patients in developing countries. Dec 2004.

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