*Original Article*

# Prevalence and patient characteristics associated with pleural tuberculosis in Nigeria

Olufemi O. Adewole, Greg E. Erhabor, Akinwumi B. Ogunrombi, Fehintola A. Awopeju

*Department of Medicine, Obafemi Awolowo University Teaching Hospitals Complex, PMB 5538, Ile Ife, Osun State, Nigeria*

**Abstract**

Background: Tuberculosis is a leading cause of mortality worldwide, with a growing death rate. The pleural space is a common extrapulmonary site of involvement.

The aim of this paper is to document prevalence and types of pleural involvement in pulmonary tuberculosis and patient characteristics associated with its occurrence.

Methodology: The study was conducted in a hospital outpatient clinic in which consecutive patients with pulmonary tuberculosis (PTB) or suspects were recruited and studied for the presence of co existing pleural disease or involvement (PD).

Results: Of 100 patients studied, eighty-two (82%) had PTB alone and six (6%) patients had PD. Pleural effusion was responsible for the majority of the cases, accounting for 67% of PD. There was no case of empyema. Mean age between patients with PTB and PTB/PD was similar. On univariate analysis, patients with PD had a shorter duration of symptoms and increased reporting of fever (p value = .0.02) and were also different from those with only PTB in HIV seropositivity and sputum smear from AFB (p value = 0.02 and 0.00 respectively). However, after adjustment for multiple comparisons using the Bonferroni test, the only significant difference between them was in the HIV seropositivity rate (p value < 0.012).

Conclusion: Less than one tenth of patients with PTB have co-existing and involvement of the pleural space. Pleural involvement is associated with HIV.

**Key words:** tuberculosis; pleural TB; Nigeria

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## Introduction

Tuberculosis (TB) continues to be a major cause of disability and death. About one third of the world's population is infected with the tubercule bacillus and the disease is responsible for 2-3 million deaths annually with a global case fatality of 27%, although it has reached up to 81% in African countries; at 6%, America has the lowest fatality rate [1,2].

Tuberculosis accounts for 2.5% of the global burden of disease and is the commonest cause of death in young women, accounting for more deaths than all other causes of maternal mortality combined [3]. It is second cause of death worldwide after HIV/AIDS, killing nearly two million people each year [3,4]. Up to75% of individuals with TB are within the economically productive age group of 15 to 54 years [5], which impairs socioeconomic development, thereby perpetuating the poverty cycle.

Tuberculosis affects almost every organ in the body, but the usual site of the disease is the lungs, accounting for more than 80 percent of tuberculosis cases [6]. Involvement of extrapulmonary sites is usually associated with increased morbidity and mortality, and with the advent of HIV, disease patterns have changed, with a higher incidence of disseminated and extrapulmonary disease now occurring [7].

Pleural involvement is a common form of extrapulmonary disease and may occur in the presence or absence of pulmonary parenchymal disease on the chest radiograph, with frequency of ranging from 3.5-30% [7-11]. Despite the high prevalence and morbidity of TB in our environment [12], and the change in disease pattern due to the HIV epidemic, there is lack of recent data on the prevalence of pleural disease in pulmonary tuberculosis (PTB) and especially factors associated with occurrence. The goal of this study was to

determine the prevalence and patient characteristics associated with concurrent development/occurrence of pleural extension in patients with PTB.

## Materials and methods

The study employed a descriptive and a cross-sectional design to investigate the prevalence and factors associated with the occurrence of pleural involvement in patients with underlying PTB. We evaluated patients seen in an outpatient setting. They were referrals to us from various clinics, such as general outpatient departments. They were either TB suspects with chronic cough or those with PTB or others whose diagnoses were uncertain to the referring physicians.

Diagnosis of PTB was made by a combination of clinical features, microscopy, histology, and chest radiograph and in line with the recommendations of the National Tuberculosis and Leprosy Control Programme of the Federal Ministry of Health, Nigeria. In summary, diagnosis of PTB was based on the presence of at least two positive smear results, or a negative smear result with radiographic features suggesting PTB and with no improvement after a course of broad spectrum antibiotics with input from a consultant experienced in TB [6].

Patients with microbiological and/or radiological evidence of PTB with additional involvement of the pleural space were categorised as those with pleural TB (PD) *i.e.,* PTB with pleural involvement, while those with pulmonary parenchymal disease only without pleural or any other extrapulmonary affectation were classified as pulmonary tuberculosis (PTB).

Patients with PTB and suspected involvement of organs outside the chest were categorised as extr pulmonary-extrathoracic TB (EPTTB). These cases were also noted and documented.

Data were collected by the use of an interviewer who administered a semi-structured questionnaire. The questionnaire investigated the socioeconomic characteristics of each patient, patients' symptoms and their duration, clinical examinations, and other information. Weight and height were measured to calculate the BMI.

Additional examination including chest radiographs, ultrasound and thoracocentesis were performed in those with suspected pleural involvement to identify effusion and/or pneumothorax. Pleural fluids were sent for microbiological and cytological studies in those with smear-negative sputum results.

Patients who had pleural involvement were analysed and compared with those with only pulmonary TB

*Statistical analysis*

Quantitative data, both categorical and continuous, were analyzed on a personal computer using the SPSS software version II. Initial data exploration was done by examining the frequency distribution of all the variables present in the questionnaire. Proportions and percentages were used to describe the socio-demographic characteristics of patients.

Chi square test was used to determine the association between socio-demographic characteristics and clinical findings between patients with PTB and those with PTB and pleural disease. Because of the small absolute number of cases, Bonferroni adjusted p values were used with significance at p values $< 0.01$. Student T- test was used to compare means of continuous variable between the two groups while analysis of variance was used for more than two groups.

## Results

One hundred patients were recruited for the study. Information and data were incomplete in four patients. Overall, 82 patients had PTB alone, while six patients had PTB and pleural involvement. Eight patients had different forms of abdominal involvement in addition to PTB.

*Patient characteristics*

Table 1 shows the socio-demographic characteristics of the patients studied. Eighty-two (82%) had PTB while 6 (6%) patients had PD. Eight patients had EPTTB. The majority of the patients were in the age group 20 to 29, constituting 47% of the subjects. There was no significant difference in the mean age of the patient groups: 32.2 $\pm$ 12.8 years versus 36.0 $\pm$ 13.9 versus 36.6 $\pm$ 6.0 for the PTB group, PTB and PD and EPTTB group respectively (p value = 0.7). Seventeen percent each of those with PD were smokers and consumed alcohol. Other characteristics of this cohort are as shown in Table 1.

*Frequency and types of pleural disease*

Of the 100 patients who were recruited, six patients had PD, giving an overall prevalence of 6%. Four patients (67%) had pleural effusion (PE) alone while two patients (33%) had PE with pneumothorax.

**Table 1.** Socio-demographic characteristics of study subjects.

| Characteristics | PTB alone n = 82(%) | PTB + pleural disease n = 6 (%) | Total n = 88 (%) |
|---|---|---|---|
| **Mean age, years** | 31.7± 12.12 | 33.8 ±11.4 | |
| **Sex** | | | |
| M | 42(51) | 4(67) | 46(52) |
| F | 40(49) | 2 (33) | 42(48) |
| **Marital Status** | | | |
| Single | 41(50) | 3(50) | 44(50) |
| Married | 41(50) | 3(50) | 44(50) |
| **Educational level** | | | |
| < 11 years | 21 | - | 21(24) |
| ≥ 11 years | 61 | 6 | 67(76) |
| Smoking, Yes (%) | 11% | 17% | |
| Alcohol, Yes (%) | 18% | 17% | |

All the PD occurred on the right hemithorax. There was no case of empyema.

*Clinical and laboratory features of PTB and PD Patients*

Table 2 compares some clinical and laboratory features between PTB patients and those with PD. On univariate analysis, there were significance differences between PTB and PD patients in mean duration of symptoms, occurrence of fever, sputum smear for AFB, and HIV seropositivity (p values < 0.05).

After adjusting for multiple comparisons using the Bonferroni test, significant association was sustained only for HIVseropositivity rate (p value < 0.016).

## Discussion

In this study, the prevalence of pleural disease in PTB was 6%, with pleural effusion alone accounting for 67% of pleural form of involvement. Pneumothorax was found in 2% of the patients and occurred in association with pleural effusion. All the cases occurred on the right hemithorax. Smoking was associated with occurrence of pleural disease. Patients who developed pleural disease had a shorter mean duration of symptoms, had a higher occurrence of smear-negative results, and increased occurrence of fever. However, the strongest and most important association found was in HIV-positive patients.

Our findings are quite similar in many respects to those reported by Aktogu *et al.* from Turkey [13]. In that study of over 5,000 patients, 6.7% of those with PTB had pleural involvement, and 6.7% and 1.5% had pleural effusion and pneumothorax respectively. Comparatively, in our study, 6% had PD and PE while 2% had pneumothorax. Our findings, however, are higher than the 3.5% recently reported in the United States [8]. These findings may be a reflection of the changing pattern in the disease spectrum/epidemiology.

The most common form of pleural tuberculosis seen in this study was pleural effusion, occurring alone in 67% of the patients and co-existing with pneumothorax in another 33%. Pneumothorax was found only in association with pleural effusion. TB pleural disease may occur following primary and secondary TB [14]. In our cases it was most likely due to post-primary TB reactivation as majority of the patients also had parenchyma affectation. Parenchyma affectation is almost always present in most cases of TB pleurisy in reactivated cases and occurs in about 30% of patients with primary TB [14]. While factors associated with the occurrence of the two forms are similar, pneumothorax tends to develops more following rupture of tuberculous cavities.

Previous investigators from Edinburgh have shown that pleural effusion tends to occur more commonly on the right hemithorax [14]. In this study, we have a similar finding both for PE and pneumothorax.

Patients co-infected with HIV are more likely to develop pleural TB, as found in this study. Both

**Table 2.** Clincial and laboratory features of patients studied

| **Characteristics** | **PTB alone n =82(%)** | **PTB + Pleural disease n = 6 (%)** | **P value** |
|---|---|---|---|
| Mean duration of symptoms( *months)* | 3.4± 4.1 | 1.75 ± 1.25 | 0.02 |
| Contact History (**Yes %**) | 18(22%) | 2(33%) | 0.7 |
| Past treatment of TB (**Yes %**) | 14(17%) 67(82%) | 1(16%) | 0.7 |
| Weight loss (**Yes %**) | 39(47%) | 6(100%) | 0.4 |
| Fever (**Yes %**) | 37(45%) | 6(100%) | 0.02 |
| Chest pain (**Yes %**) | 17.4±2.3 | 2(33%) | 0.5 |
| Mean BMI ($Kg/m^2$) | 34.4± 4.7 | 17.7± 2.3 | 0.7 |
| Mean PCV (%) | 79.7± 36.5 | 36.0 ± 2.8 | 0.4 |
| Mean ESR(mm/hr) | | 84.3± 37 | 0.7 |
| Sputum AFB (**Pos %**) | 70(85%) - | 3(50%) | 0.02 |
| HIV Positivity (%) | | 2(33%) | 0.00 |

BMI (Body mass index), PCV (Packed Cell Volume) and ESR (Erythrocyte sedimentation rate), AFB (Acid fast bacilli) and HIV (Human Immuno deficiency Virus)

forms are associated with HIV positivity. In one study, pleural reaction was seen in 37% of HIV patients with TB, while pleural effusion was seen in 11% of HI- negative patients with TB [15]. The effects of HIV and PTB co-infection may be synergistic in the occurrence of pleural disease. Pleural TB incidence may also be impacted by co-infection with HIV [8].

Diagnosis of pleural TB, whether pleural effusion or pneumothorax, can be made reasonably on clinical grounds, though radiological, microbiological or histological investigations are necessary for confirmation.

In this study, about half the patients with pleural TB had positive sputum smears for AFB compared with 87% of those with PTB. This finding is consistent with the observations of Haa [16], where sputum smears were positive in 50% and cultures were positive in 60% of those with tuberculous PD. These results could be due to co-existing parenchyma disease, as commonly seen in most post-primary disease. However, in primary pleural TB, sputum smears are rarely positive and cultures are positive in only 25-33% of patients [16].

Early diagnosis is the key to successful management. Microbiological confirmation is essential to diagnosis. Other diagnostics tests such as the pleural adenosine deaminase level, tuberculostearic acid, polymerase chain reaction, and pleural biopsy could greatly improve and enhance early diagnosis. In the absence of these tests, a high index of suspicion based on epidemiology of TB, presence of HIV, lymphocytic predominance on pleura effusion, and in some situations response to anti-TB may be useful for presumptive diagnosis.

This study faced some limitations, including small sample size, recall bias for symptoms and their duration, and unavailability of pleural biopsy results. We were also not able detect other pathologies in the pleural surface such as subpleural blebs. Ultrasound and/or computed tomography of the chest would have been useful in those cases, though cost may be an issue in future investigations. More studies will be needed to determine the diagnostic utilities and correlation of various biomarkers, pleural biopsy results, and AFB culture in diagnosing tuberculous pleural effusion in our environment.

Despite these limitations, this study has shown that patients who develop pleural TB are not different in age, sex, social class, and anthropometric characteristics compared with those with PTB alone. A short history of symptoms and HIV-positive status may be useful pointers to the occurrence or existence of pleural involvement in TB.

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## Corresponding author

Dr. Olufemi O. Adewole
Department of Medicine
Obafemi Awolowo University Teaching Hospitals Complex
PMB 5538, Ile Ife, Osun State, Nigeria
Email: adewolef@yahoo.co.uk

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