Extra-Pulmonary Tuberculosis Among Patients Managed for Tuberculosis at a Tertiary Health Care Institution in South-West Nigeria: A Retrospective Study

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Abstract

Background

Tuberculosis (TB) is a cause of high morbidity and mortality across the world but more so in developing countries. A large proportion of patients with tuberculosis present with extra-pulmonary disease which is often misdiagnosed or under-diagnosed. In Southwest Nigeria, there are reports on tuberculosis but only a few focused on extra-pulmonary tuberculosis (EPTB). This study was aimed to determine the burden of EPTB and its associated factors in a tertiary health care centre in Nigeria.

Methods

This was a cross-sectional retrospective study involving all the TB cases seen from 1st January 2015 and 31st December 2019. Relevant information was retrieved from the clinical records of the patients with the use of a well-structured proforma. Data obtained was analysed using the Statistical Package for Social Sciences (SPSS) version 23.0.

Results

Five hundred and nine subjects were involved with a mean age of 39.8±16.99 years. Three hundred and sixteen (62.1%) were males, 69 (13.6%) participants were HIV positive. Eighty-three (16.3%) had EPTB, of these 32 (38.6%) had spinal tuberculosis while 23 (27.7%) had pleural tuberculosis. Age, new cases of TB, and smear-negative TB were found to be significantly associated with the development of EPTB.

Conclusion

Extra-pulmonary tuberculosis is a common form of tuberculosis in our community, and the commonest presentation is spinal and pleural tuberculosis. There is a need for an improvement in diagnostic capacity for EPTB especially among the middle-aged and those presenting with TB for the first time. This will aid in the prompt detection and management of patients with EPTB.

Introduction

Tuberculosis (TB) is a global emergency, a major cause of death worldwide, especially in people with secondary or coexisting illnesses such as Human Immunodeficiency Virus (HIV) (1). This disease is caused by *Mycobacterium tuberculosis* and people who are infected by tubercle bacilli have about a 10% chance of developing tuberculosis in their lifetime (1)(2). Presently, about a quarter of the world's population is infected with *Mycobacterium tuberculosis* and thus at risk of developing tuberculosis (1).

In 2018, about 10 million new cases of tuberculosis were reported from all regions of the world and eight countries accounted for two-thirds of the global total record: India (27%), China (9%), Indonesia

(8%), the Philippines (6%), Pakistan (6%), Nigeria (4%), Bangladesh (4%) and South Africa (3%). These and 22 other countries in WHO's list of 30 high tuberculosis burden countries accounted for 87% of the world's cases (1).

There are many recent advances in diagnosis and treatment of *Mycobacterium tuberculosis* infection, and tuberculosis prevalence is on the decline worldwide (3). However, the prevalence of this disease is still high in some low-income and middle-income countries (3). The persistent high prevalence is due to the higher incidence of drug resistance in *Mycobacterium tuberculosis,* and co-infection with HIV. Also, poverty, with resulting indices such as overcrowding, malnutrition, and inability to access appropriate health care is responsible for the high disease burden in these countries (1)(3).

Extra-pulmonary tuberculosis (EPTB) is tuberculosis occurring at any other tissue or organ in the body apart from the pulmonary parenchyma (4)(5). Although the commonest sites are lymph nodes, pleura, and osteoarticular systems, this disease can occur in any organ of the body (4)(5). Up to 25% of tuberculosis cases present as extra-pulmonary disease and it is usually from haematogenous or lymphatic spread of the bacilli to other organs (4)(5).

Diagnosis of EPTB might be difficult as the presentation is not usually classical, it might mimick other diseases (6)(7) . Thus, specimens obtained from such sites of infection might not be routinely sent for *Mycobacterium tuberculosis* diagnostic assessment in the laboratory. The samples collected could also be paucibacillary, because obtaining a representative specimen through the sampling of sites involved might be a difficult process. Histologic diagnosis is often the gold standard for EPTB(6)(7). Delay in diagnosis or misdiagnosis of patients with EPTB could result in a poor disease outcome (6)(7).

Some factors such as female gender, black race, and co-morbidities such as positive HIV status have been associated with EPTB in some scientific studies from developed countries such as United States, Taiwan, Turkey, and Portugal (8)(9)(10)(11). However, available data from West Africa have not reported all of these factors as recognized risks in patients who presented with EPTB(12)(13)(14).

This study investigated retrospectively the burden of EPTB and its associated factors in the patients managed for tuberculosis at Bowen University Teaching Hospital Ogbomoso in Southwest Nigeria over a period of five years.

Materials And Methods

Study Site

The study was carried out at TB/DOTs clinic of Bowen University Teaching Hospital (BUTH) Ogbomoso. This clinic is supported by the National Tuberculosis and Leprosy control programme. On account of its location within BUTH which is a tertiary health centre, the clinic serves the people residing within its locality. It also serves people from across neighbouring towns.

Ogbomoso is located on latitude 8” 08’ 00” East and longitude of 4”16’ 00” North of the Equator and is the second-largest city in Oyo State after Ibadan the capital of Oyo State.

Study Design

This was a retrospective cross-sectional study. The records of all patients, including children who were managed for tuberculosis between 1st January 2015 and 31st December 2019 at BUTH were included in this study.

Data Collection

We collected data from the tuberculosis Directly Observed Treatment Short-Course (DOTS) treatment center and from the clinical records of the patients. The patients were managed and followed up at the treatment clinic after a diagnosis of tuberculosis had been established. Diagnosis of tuberculosis in the patients was by detection of *Mycobacterium tuberculosis* either by Ziehl Neelsen staining, fluoresce staining technique, or Gene Xpert MTB/RIF assay done on the clinical specimen from site of infection and by radiological confirmation. Also, some diagnoses were made based on clinical judgement of managing Physicians as recommended by WHO(15).

Data was collated with the use of a well-structured proforma and relevant information on subjects with tuberculosis was classified under the following headings: biodata and demographic information, results of investigations, and treatment outcome.

An effort was made to avoid double data entry and all database was kept strictly confidential.

Ethical Statement

Ethical approval for the study was gotten from the Ethics and Research Committee of BUTH, Ogbomoso.

Definition of terms (according to the WHO)(15).

TB case: Either a bacteriologically confirmed biological specimen positive by either smear microscopy or GeneXpert, or clinically diagnosed with TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment.

Successfully treated: Good treatment outcome

Poor treatment outcome: This refers to patients who either died, or were lost to follow-up or had treatment failure.

Death: A TB patient who died for any reason before starting or during the course of treatment.

Lost-to-follow-up: A patient who did not start treatment or treatment interrupted for 2 consecutive months or more.

Treatment failure: A patient whose sputum smear or culture is positive at month 5 or later during treatment.

Statistical Analysis

The data obtained were analysed using the Statistical Package for Social Sciences (SPSS) version 23.0 (SPSS Chicago Inc., IL, U.S.A). Continuous variables were expressed as means ± standard deviation [SD]. Frequency distribution tables were used for categorical variables. The relationship between categorical variables was determined using chi-square. A p-value equal to or less than 0.05 was considered significant.

Results

The clinic had a total of 524 TB cases during the five years Fifteen of these were excluded from the analysis because they were transferred to other centers to complete their treatment on account of proximity to their places of abode; hence, 509 TB cases were analysed. The patient age range was between 1 and 90 years, with a mean age of 39.8±16.99 years. There were 316 (62.1%) males, and 69 (13.6%) patients had HIV co-infection (Table 1). Eight-three (16.3%) of the subjects had EPTB. Of these, 32 (38.6%) had TB spine, 23(27.7%) had pleural tuberculosis, 9 (10.8%) had abdominal and 10 (12%) patients presented with disseminated TB. There were three (3.6%) cases each of TB meninges and TB adenitis, two patients had TB pericarditis and there was only one case of miliary TB. (Table 2). Age, treatment category (new cases/retreatment), non-detection of *Mycobacterium tuberculosis* from clinical specimen, and treatment outcomes were significantly associated with the occurrence of extrapulmonary TB (Table 3). There was no significant association between gender, HIV status, rifampicin resistance, and EPTB.

Table 1: Characteristics of the TB patients

Variables	Frequency (n) n=509	Percentage (%)
Age (in years)		
1 – 20	68	13.4
21 – 40	223	43.8
41 – 60	153	30.1
61 – 80	61	12.0
81 – 100	4	0.8
Gender		
Male	316	62.1
Female	193	37.9
HIV status		
Positive	69	13.6
Negative	440	86.4
Treatment category		
New case	455	89.4
Re-treatment	54	10.6
MTB detected		
Yes	359	70.5
No	120	29.5
Rifampicin Resistance		
Yes	9	1.8
No	500	98.2
Outcome		
Successfully Treated	426	83.7
Died	62	12.2
Lost to follow-up	7	1.4
Treatment failure	14	2.8

Table 2: Extra-pulmonary TB among the subjects

Variable	Frequency (n)	Percentage (%)
Extra-pulmonary TB (n=509)		
Yes	83	16.3
No	426	83.7
Types of extra-PTB (n=83)		
TB spine	32	38.6
TB meningitis	3	3.6
Pleural TB	23	27.7
Miliary TB	1	1.2
TB pericarditis	2	2.4
TB abdomen	9	10.8
Disseminated TB	10	12.0
TB lymphadenitis	3	3.6

Table 3: Relationship between Subjects' Characteristics and the Occurrence of EPTB

Variables	Extrapulmonary TB		Test statistics	p-value
	Yes, n (%) n=71	No, n (%) n=329		

Age				
1 – 20	16 (23.5)	52 (76.5)	χ2=14.646	**0.005**
21 – 40	23 (10.3)	200 (89.7)		
41 – 60	28 (18.3)	125 (81.7)		
61 – 80	16 (26.2)	45 (73.8)		
81 – 100	0 (0.0)	4 (100.0)		
Gender				
Male	51 (16.1)	265 (83.9)	χ2=0.017	0.896
Female	32 (16.6)	161 (83.4)		
HIV status				
Positive	13 (18.8)	56 (81.2)	χ2=0.376	0.540
Negative	70 (15.9)	370 (84.1)		
Treatment category				
New	82 (18.0)	373 (82.0)	χ2=9.248	**0.002**
Re-treatment	1 (1.9)	53 (98.1)		
MTB detected				
Positive	16 (4.5)	343 (95.5)	χ2=125.337	**0.000**
Negative	67 (44.7)	83 (55.3)		
Rifampicin Resistance				
Yes	2 (22.2)	7 (77.8)	χ2=0.235	0.628
No	81 (16.2)	419 (83.8)		
Outcome				
Successfully treated	65 (15.3)	361 (84.7)	LRχ2=10.203	**0.017**
Died	17 (27.4)	45 (72.6)		
Lost to follow-up	1 (14.3)	6 (85.7)		
Treatment failure	0 (0.0)	14 (100.0)		

Discussion

In this study, we described the factors observed in patients with extra-pulmonary tuberculosis (EPTB) from a total of 509 patients with tuberculosis who were treated at our center and were involved in this study. Out of 509 patients, 83 (16.3%) were found to have EPTB, this finding is similar to reports from previous studies on tuberculosis done in Nigeria and outside Nigeria which reported prevalence between 9% and 32% (16)(12)(9)(13)(17). Although it is lower than the prevalence reported from some other regions, it could be due to regional differences in the prevalence of tuberculosis and could also be a result of differences in diagnostic capacity. Centers with more advanced clinical, radiological, and laboratory support are more likely to make a diagnosis of EPTB (7).

The mean age for patients with EPTB has been reported to be higher than those with pulmonary tuberculosis(17). A significant association (p= 0.005) was found between age and the occurrence of

EPTB in this study, with a bimodal peak observed in the age distribution of those with EPTB. Those between 21-40 years and 41-60 years had the highest presentation, both accounting for 61.5% of the total cases. There were no cases of EPTB in the geriatric age group above 80 years, which is not surprising as pulmonary tuberculosis is said to be commoner than EPTB in this age group(18).

Although there was no significant association between gender and EPTB from our study, the majority of the patients managed for tuberculosis, both pulmonary tuberculosis and EPTB at our center were males (n= 316, 62.1%). Some studies from Africa and some done outside Africa reported female sex to be a risk factor in the development of EPTB (13)(12)(13)(17). However, a report from Northern Nigeria found a higher prevalence of EPTB in men than women (16). It is important to note that some of the studies with reports of a higher rate of EPTB in women were done among people of different races, these included women of black race origin who could have emigrated from a tuberculosis endemic region. Also, the local prevalence of tuberculosis in men and women could be responsible for the regional variations in the cases of EPTB found in them.

An association between HIV infection, tuberculosis, and EPTB had been established in literature over the years (8)(9)(12)(13). Sixty-nine of our patients representing 13.6% of the total study group were found to be HIV positive at presentation for treatment for tuberculosis at our center. Of these, 13 (18.8%) had EPTB. There was however no significant association between HIV status and EPTB in this study. A study done in the North-Eastern part of the country also found a lower prevalence of EPTB in patients living with HIV (16).

A significant association was observed between treatment categories and the occurrence of EPTB in this study (p=0.002). The majority (n=82, 98.8%) of the patients who had EPTB at our center were newly diagnosed with tuberculosis. This would explain the overall successful treatment outcome for these patients, as most recovered fully on first-line anti-tuberculous therapy under DOTS.

There was a significant association (p=0.000) between detection of *Mycobacterium tuberculosis* from clinical specimen and EPTB. A majority (n=359, 70.5%) of the patients involved in this study were smear-positive. However, 82.7% (n=67) of the patients with EPTB were smear-negative, and *M. tuberculosis* was not detected in the samples of these patients by all methods used. Diagnosis in these patients is majorly by clinical assessment, and by radiological methods especially for those with spine TB. This is an important factor and could be responsible for lower cases of reported EPTB not only at our centre but also in other regions which rely more on clinical and radiologic evidence in the diagnosis of EPTB(7).

Tuberculosis of the bone especially the spine has been reported in several articles from different climes as very common, while some reported it as the commonest form of EPTB(16)(4)(18)(17). TB spine is common as a result of previous hematogenous foci, or a contiguous disease, it could also be by lymphatic spread from pleural disease (2). At our centre, we found tuberculosis of the spine was the commonest presentation of the EPTB cases seen in 38.6% of the patient. Pleural tuberculosis was also fairly common among the patients; it was diagnosed in 27.7% of the patients. Tuberculous adenitis was found in 3 (3.6%) patients, and this is lower than another report from Northern Nigeria(16). This is

probably because the mean age of the patients in this study is 39.8±16.99 years and lymph node tuberculosis has been documented to be more frequently found in children(4) (10)(18).

Conclusion

Overall, from this study, we found that EPTB is a common form of tuberculosis in our environment. It is found more among the middle-aged, smear-negative, and new cases of TB. The commonest presentations are spinal and pleural tuberculosis.

List Of Abbreviations

TB – Tuberculosis

EPTB – Extra-pulmonary tuberculosis

DOTS- Directly Observed Treatment, Short-Course

BUTH – Bowen University Teaching Hospital

SPSS – Statistical Package for Social Sciences

HIV – Human Immunodeficiency Virus

WHO – World Health Organization

Declarations

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Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

AR, AO and AO were involved in data collection, processing, analysis, interpretation of data and major contributors in writing the manuscript. AA also contributed to writing the manuscript.

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Data Availability Statement

The datasets used and/or analysed during the study are available from the corresponding author on reasonable request.

Disclaimer

The views expressed in this article are those of the authors and not an official position of the Institution.

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