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High proportion of extrapulmonary tuberculosis in a low prevalence setting: a retrospective cohort study

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Abstract

Objectives—The proportion of extrapulmonary tuberculosis (EPTB) cases in the United States (US) has been rising due to a slower rate of decline in EPTB compared to pulmonary tuberculosis (PTB). The purpose of this study was to characterize the clinical and treatment differences between EPTB and PTB patients, and identify patient factors associated with EPTB.

Study Design—We performed a retrospective cohort study of active tuberculosis (TB) cases treated at the Baltimore City Health Department between 2008 and 2013.

Methods—We categorized patients as having “only PTB” (infection in the lung parenchyma), “EPTB/PTB” (infection in the lung and an additional site), and “only EPTB” (infection not involving the lung). Pearson's χ squared tests were used to evaluate categorical variables and compare clinical and demographic differences between only PTB, only EPTB, and EPTB/PTB patients. Student t-tests and one-way analysis of variance tests were utilized to assess continuous variables and to compare treatment differences.

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Results—One hundred and sixty-three patients were treated for TB; 39.3% had some form of EPTB (either EPTB/PTB or only EPTB). There was no difference found between EPTB, PTB, and EPTB/PTB patients with respect to HIV status, gender, race, foreign-born status, or mean age. Patients with only EPTB were less likely than patients with some form of PTB (only PTB or EPTB/PTB) to present with cough (30.4% vs. 61.5%; $p<0.001$), night sweats (10.9% vs. 39.3%; $p<0.001$), and weight loss (28.3% vs. 47.9%; $p=0.023$). Patients some form of EPTB were also more likely to be hospitalized post-diagnosis compared to patients with only PTB (39.1% vs. 20.2%; $p=0.009$), and to have longer mean durations of treatment (37.9 weeks [SD=11.1] vs. 31.8 weeks [SD=8.1]; $p<0.001$).

Conclusions—EPTB patients present with atypical symptoms, undergo prolonged treatment, and experience increased hospitalizations. In order to improve diagnostic algorithms and treatment modalities, EPTB must be further characterized.

Keywords

Tuberculosis; Extra pulmonary tuberculosis; Baltimore City; Foreign born

Introduction

Tuberculosis (TB) remains a public health concern in the United States (US), despite recent decreases in incidence[1]. Nationally there are 3.0 cases of TB per 100,000 persons; while this is a significant improvement from the country's rate of 10.4 in 1992, it is still far from the goal of TB elimination (<1 case per 100,000)[2].

While the national rates of TB have been steadily improving in the last decade, the rate of decline of extrapulmonary TB (EPTB) has been slower that of pulmonary TB (PTB)[3]. As such, the proportion of TB cases in the US that are EPTB has been increasing; in 2013 21% of all TB cases were EPTB, compared to approximately 16% in 1993[2-5]. It has been hypothesized that this slower reduction in EPTB cases is due to an increased prevalence of proposed risk factors for EPTB, such as HIV, foreign-born status, and advanced age[3]. Failure to identify and adequately treat EPTB can lead to the development of disseminated disease (including PTB) and the development of multidrug-resistant TB; however, few studies have examined risk factors for EPTB in the US, and even less have done so since the beginning of the antiretroviral therapy (ART) era[3-7].

Baltimore City is an urban area in Maryland with a population of approximately 620,000[8]. TB in Baltimore is a public health concern; the annual case incidence in 2013 was 3.9 per 100,000, which exceeds the national average[1, 8]. Challenges to TB control in Baltimore include high rates of homelessness, HIV infection, and substance abuse[9-11]. In addition, like many public health departments, the Baltimore City Health Department (BCHD) has limited resources. Cases of EPTB in public health settings (such as the BCHD) present additional challenges to TB control programs that have historically focused on the care of PTB patients[12].

While the general epidemiology of EPTB has been characterized at the national level, only one prior study has examined differences in presenting symptoms between PTB and EPTB

patients in the US, and no prior studies have examined differences in length of treatment and hospitalizations[3, 7]. Such information is important for clinicians and TB programs that care for patients with EPTB. The purpose of this study was to determine the burden of EPTB in Baltimore City, characterize clinical and treatment differences between EPTB and PTB patients, and identify patient-specific factors associated with EPTB. Persons with active TB treated at the BCHD between January 2008 December and 2013 were included in the study.

Methods

Study Design

We performed a retrospective cohort study of all microbiologically and clinically diagnosed active TB cases treated at the BCHD between January 2008 and December 2013. We abstracted data from both the BCHD electronic database and paper charts; demographic variables (age, sex, and country of birth, HIV status), presenting symptoms, site of disease, microbiological data, and treatment outcomes were collected.

Cases were categorized by site of disease. We determined the burden of EPTB within Baltimore city by reporting the proportion of patients with EPTB alone or in combination with PTB. TB within the lung parenchyma exclusively was classified as “only PTB,” while cases with TB exclusively involving any organ outside of the lungs were classified as “only EPTB;” cases with both pulmonary and extrapulmonary disease were categorized as “EPTB/PTB.” Additional analyses were conducted in which cases were classified as having “some form of EPTB” (either only EPTB or EPTB/PTB) and “some form of PTB” (either only PTB or EPTB/PTB). EPTB cases were further characterized based on their primary site of disease (pleural, lymphatic, central nervous system, musculoskeletal, gastrointestinal, and pericardial). Individuals with more than one site of involvement were classified based on the site with greater amount of disease during chart review.

Statistical Analyses

Statistical analysis was performed using STATA version 12.1. Pearson's χ squared tests were used to evaluate categorical variables and compare clinical and demographic differences between only PTB, only EPTB, and EPTB/PTB patients. Student t-tests and one-way analysis of variance tests were utilized to assess continuous variables and to compare differences in treatment. Patients who lacked treatment completion data due to death, transfer out of the BCHD jurisdiction, and being on treatment at the time of analysis were excluded from the analyses of treatment outcomes and treatment duration. In addition, one patient who was diagnosed with multidrug-resistant TB (MDR-TB) during the study period was also excluded from the analyses. Multivariate logistic regression analyses were used to evaluate risk factors associated with EPTB. Covariates for inclusion in the multivariate model were selected on the basis of clinical relevance and interest and included age, gender, foreign-born status, and HIV status.

The institutional review boards of the Johns Hopkins University School of Medicine and the Baltimore City Health Department approved the study.

Results

Patient Demographics

A total of 163 TB cases were treated at BCHD during the study period; 99/163 (60.7%) of cases were only PTB, 46/163 (28.2%) were only EPTB, and 18/163 (11.0%) were EPTB/PTB (Table 1). There was no statistically significant difference in the proportion of cases with EPTB or EPTB/PTB by year of presentation (p=0.813). The majority of patients were male (100/163 [61.4%]), while 102/163 (62.6%) were African-American. The mean age of presentation was 47.3 (SD=20.3). while themedian age of presentation was 45 years (IQR 30-64). Foreign-born individuals made up 44% (72/163) of all patients, with 47.0% (34/72) originating from Asia and 22% (16/72) originating from Africa. Overall, foreign-born patients were significantly younger than US-born patients (mean age 38 years [SD=17.6] for foreign-born patients and 54 [SD=19.3] for US-born patients, respectively; p<0.001); there were no other demographic differences between foreign-born and US-born patients.

In terms of diagnosis, 126/163 (77.3%) of cases had a positive microbiologic study (smear, culture, or nucleic acid amplification testing), while 5/163 patients (3.1%) were diagnosed via pathology alone. A clinical diagnosis (without any microbiologic or pathologic confirmation) was made in 32/163 (19.6%) cases. Over half of the sample was hospitalized at the time of diagnosis (52.2% [85/163]).

Out of the 163 patients in the sample, 7 people transferred out of the BCHD program prior to treatment completion, 3 were lost to follow up (defaulted), and 5 were still on treatment at the time of analysis. We therefore had treatment outcome data available for 148 patients; 20/148 (13.4%) of patients died during treatment (2 prior to treatment initiation), while the rest were cured.

HIV infection was present in 20/168 (12.8%) patients; there were 9 people in the sample whose HIV status was not known. Persons living with HIV (PLWH) were significantly more likely to have an outcome of death compared to patients without HIV or with an unknown HIV status (7/19 [36.8%], 12/121 [9.9%], and 1/8 [12.5%] for PLWH, HIV-uninfected, and HIV-unknown persons, respectively; p=0.006).

Comparison of PTB, EPTB, and EPTB/PTB cases

There were no significant differences found between only EPTB, only PTB, and EPTB/PTB patients with respect to HIV status, gender, race, foreign-born status, or mean age of presentation. However, there was a trend towards an increased proportion of EPTB/PTB patients having HIV infection (5/18 cases [27.8%]) compared to those with only EPTB (4/46 [8.7%]) and only PTB (11/99 [11/1%]; p=0.182). In terms of diagnosis, less individuals with only EPTB had a microbiological diagnosis than those with some form of PTB (32/46 [69.6%] versus [vs.] 94/117 [80.3%]), respectively, though this did not reach statistical significance (p=0.126). Patients with only EPTB were also more likely to be diagnosed on the basis of pathology alone, compared to patients with some form of PTB (4/46 [8.7%] vs. 1/117 [0.85%], respectively; p=0.022). Alternatively, more individuals with disseminated disease at multiple sites (i.e. EPTB/PTB) had a microbiological confirmation than those with

either only PTB or only EPTB (17/18 [94.4%] for EPTB/PTB, 77/99 [77.8%] for only PTB, and 32/46 [69.6%] for only EPTB, respectively) although this did not reach statistical significance (p=0.158).

For patients with only EPTB, the most common site of disease was the lymphatic system (14/46 [30.4%]), followed by pleural disease (11/46 [23.9%]), musculoskeletal disease (9/46 [19.6 %]), and then central nervous system (CNS) disease (7/46 [15.2%]). There was a significant difference in the sites of EPTB comparing those with and without HIV (p<0.001); patients with HIV were more likely to present with CNS TB (5/20 [25%]) or miliary TB (2/20 [10%]) compared to those without HIV (2/134 [1.5%] and 1/134 [0.8%] for CNS TB and miliary TB, respectively).

Differences in symptom presentation were noted between groups (Table 2). Patients with only EPTB were significantly less likely to present with cough than those with some form of PTB (14/46 [30.4%] for only EPTB vs. 72/117 [61.5%] for some form of PTB; p<0.001). They were also less likely to have night sweats (5/46 [10.9%] vs. 46/117 [39.3%]; p<0.001) and weight loss (13/46 [28.3%] vs. 56/117 [47.9%]; p=0.023) than patients with some form of PTB. In addition, patients with only EPTB were significantly more likely to have lymphadenopathy than patients with some form of PTB (14/46 [20.4%] for only EPTB vs. 8/117 [6.8%] for some form of PTB; p<0.001), and back pain (3/46 [6.5%] vs. 1/117 [0.9%]; p=0.035).

While we did not find any statistically significant differences between the site of TB and being hospitalized at the time of diagnosis, there was a trend towards patients with some form of EPTB being hospitalized more at diagnosis than patients with only PTB (37/64 [57.8%] vs. 48/99 [48.5%] for some form of EPTB and only PTB, respectively; p=0.244). Patients with some form of EPTB were also significantly more likely to have subsequent hospitalizations after they had initiated TB care compared to those with only PTB (25/64 [39.1%] vs. 20/99 [20.2%] for some form of EPTB and only PTB, respectively; p=0.009).

Regarding treatment differences, patients with some form of EPTB had statistically significantly longer mean durations of treatment compared to those with only PTB (mean of 37.9 weeks [SD=11.7] for patients with some form of EPTB and 31.8 weeks [SD=8.1] for patients with only PTB; p<0.001). There was a significant difference in treatment duration among those with some form of EPTB based on site of disease (p<0.001), with 100% of CNS TB cases, 89% of musculoskeletal TB cases, and 66% of miliary TB cases requiring treatment beyond the standard 6 month duration for uncomplicated PTB (mean 58.5 weeks [SD=9.2], 50.3 weeks [SD=11.1], and 42 weeks [SD=13] for CNS, musculoskeletal, and military TB, respectively [Table 3]). There was also a significant difference between patients with regards to the ordering of treatment extensions (an additional 12 weeks or more of therapy beyond the initial planned treatment duration); 22/80 (27.5%) of only PTB patients, 13/32 (40.6%) of only EPTB patients, and 9/15 (60%) of EPTB/PTB patients received extensions (p=0.037).

There were no statistically significant differences seen with regard to treatment outcome between patients; a higher proportion of patients with only EPTB had an outcome of death

compared to patients with only PTB and EPTB/PTB, but this did not reach statistical significance (8/40 [20.0%], 10/91 [11.0%], 2/17 [11.8%] for only EPTB, only PTB, and EPTB/PTB, respectively; p=0.371).

On multivariate analysis, we did not identify any risk factors associated with EPTB after adjusting for age, sex, foreign-born status, and HIV status

Discussion

Our study shows that between 2008-2013, 39.3% of TB cases in Baltimore City had some form of EPTB, while 28% of cases had only EPTB without evidence of pulmonary disease. In contrast to some prior reports, we did not find temporal changes or increases in the proportion of patients with EPTB; rather we found consistently large proportions of EPTB during the study period[3]. Overall, these results appear to indicate a higher EPTB period prevalence in Baltimore City compared to the 21% prevalence recorded in the national data[3]. These findings have implications for public health TB programs in terms of resource allocation. Our study found that patients with EPTB have atypical symptoms that may go unrecognized by clinicians; they also required more extensive diagnostics (e.g. tissue pathology) and longer treatment durations.

We did not observe any difference between only PTB patients, only EPTB patients, and EPTB/PTB patients with respect to age, sex, race, or foreign-born status. These findings are important and indicate that it may not be possible to generate simple algorithms to identify individuals at higher risk for EPTB. While our finding that foreign-born status is not a risk factor for EPTB contrasts with prior work, this may be due to the relatively lower proportion of TB among foreign-born persons in Baltimore City compared to other areas in Maryland (and the nation)[3, 4, 6, 13, 14]. Nonetheless, our findings in this regard are not unique; Gonzales et. al similarly did not find an association between EPTB and foreign-born status in Houston[7]. By contrast, other non-national database studies that have suggested an association between EPTB and foreign-born status have been restricted to data from rural settings, or among PLWH[4, 6].

Several prior studies have also demonstrated an increased prevalence of EPTB infection in patients with immunologic deficiencies in the US, specifically HIV co-infection[4, 5, 15-17]. Interestingly, while there was a trend towards more HIV infection in our patients with EPTB/PTB, we did not find any significant associations; we also did not observe a trend towards more HIV infection in our EPTB patients. This may have been a result of the relatively small number of PLWH in our study; however, it is also possible that our findings represent a changing epidemiology of EPTB in the US in the era of greater access to and usage of ART for HIV. Much of the prior work characterizing the epidemiology of EPTB in the US was either done prior to the ART era, or examined a time period that included years during which ART was not readily available. Additional larger studies are necessary to determine if the epidemiology of EPTB has changed in recent years.

With regards to disease presentation, our results suggest that the majority of individuals with EPTB do not present with symptoms that are considered characteristic for TB (e.g. cough,

night sweats, etc.). The only other study to examine symptom differences among EPTB and PTB patients in the US also found a paucity of “classic” TB symptoms; this implies that our findings may potentially be generalizable to other TB programs[7]. As a lack of traditional symptoms could lead to delays in diagnosis, this is important for TB programs; clinicians must maintain a high index of suspicion for EPTB when patients present with atypical symptoms[18]. In addition, clinicians must be aware of the potential diagnostic challenges for patients who have isolated EPTB without PTB. To our knowledge, this is the first study in the US to examine differences in microbiologic diagnoses between PTB and EPTB patients; our data show that individuals with only EPTB had higher proportions of diagnoses based on pathology alone. Providers should know that the diagnosis of EPTB in the absence of PTB may require a more intensive evaluation.

To our knowledge this is also the first study done in the US to examine differences in hospitalization patterns and treatment durations between EPTB and PTB patients. Our patients with only PTB received a mean of nearly 32 calendar weeks of treatment; this includes the time needed to make up missed doses and complete the standard 6-month course, but also represents the need for treatment extension in some individuals with extensive disease and/or slow treatment response. Despite this, patients with the presence of some form of EPTB were still treated for a significantly longer period of time than only PTB patients (37.9 weeks). This finding alone is not surprising, given that some sites of EPTB disease are recommended to receive longer durations of treatment than PTB (such as CNS disease)[18-20]. However, we also found that compared to patients with only PTB, those with only EPTB and EPTB/PTB required more treatment extensions beyond what was initially planned. This implies that such patients are receiving longer lengths of treatment than was expected for their site of disease. However, due to our sample size we were unable to compare specific sites of EPTB to PTB in terms of treatment duration; larger studies are needed to examine this. We also found that patients with some form of EPTB were more likely to have subsequent hospitalization during treatment (i.e. hospitalization beyond those during initial diagnosis); such hospitalizations require increased capital from health systems. While reasons for hospitalization were not consistently available during this study, these findings may suggest that patients with EPTB have more treatment complications or greater disease severity requiring inpatient management. Our findings thus demonstrate that increased resources must be directed towards the care of patients with EPTB, which is significant in an era of both public health and health system budget constraints.

Our study has several limitations. First, Baltimore city is an urban environment of medium size with a relatively low absolute number of TB cases; as such, our findings may not be generalizable to cities of larger size, or low/middle-income countries where TB incidence is higher. Nonetheless, we provided detailed analyses that will aid clinicians and public health officials in low TB-prevalence settings in directing resources towards a goal of TB elimination. As with all retrospective analyses, our primary source data was collected for clinical or public health purposes, rather than for research; we were therefore limited in the number of clinical and demographic patient-specific factors that could be assessed when comparing individuals with and without EPTB. However, we conducted detailed chart reviews and provide important insights into the diagnosis and treatment of EPTB patients in

a public health TB program. Given relatively small sample size, our ability to conduct comparisons among subgroups was limited.

Our work shows that there is a significant burden of EPTB in Baltimore, and that patients with EPTB have different presentations, diagnostic needs, and treatment courses than patients with PTB. In addition, EPTB represents a challenge to financially limited health departments due to prolonged treatment and increased hospitalizations. In order to improve diagnostic algorithms and treatment modalities, EPTB must be further characterized.

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References

1. World Health Organization. [cited 2015 Oct 4] Towards tuberculosis elimination: an action framework for low-incidence countries. 2015. Available from: http://www.who.int/tb/publications/elimination_framework/en/
2. Centers for Disease Control and Prevention (CDC). [cited 2015 Oct 4] Reported tuberculosis in the United States, 2013. 2015. Available from: http://www.cdc.gov/features/dstuberculosis
3. Peto HM, Pratt RH, Harrington TA, LoBue PA, Armstrong LR. Epidemiology of extrapulmonary tuberculosis in the United States, 1993-2006. Clin Infect Dis. 2009; 49:1350–1357. [PubMed: 19793000]
4. Kipp AM, Stout JE, Hamilton CD, Van Rie A. Extrapulmonary tuberculosis, human immunodeficiency virus, and foreign birth in North Carolina, 1993 - 2006. BMC Public Health. 2008; 8 107-2458-8-107.
5. Yang Z, Kong Y, Wilson F, Foxman B, Fowler AH, Marrs CF, et al. Identification of risk factors for extrapulmonary tuberculosis. Clin Infect Dis. 2004; 38:199–205. [PubMed: 14699451]
6. Wohl AR, Lu S, Rollins JN, Simon PA, Grosser S, Kerndt PR. Comparison of AIDS progression and survival in persons with pulmonary versus extrapulmonary tuberculosis in Los Angeles. AIDS Patient Care STDS. 2001; 15:463–471. [PubMed: 11587632]
7. Gonzalez OY, Adams G, Teeter LD, Bui TT, Musser JM, Graviss EA. Extra-pulmonary manifestations in a large metropolitan area with a low incidence of tuberculosis. Int J Tuberc Lung Dis. 2003; 7:1178–1185. [PubMed: 14677893]
8. Maryland Department of Health and Mental Hygiene. [cited Oct 4 2015] Maryland TB Statistics. 2013. Available from: http://phpa.dhmh.maryland.gov/OIDPCS/CTBCP/SitePages/Statistics.aspx
9. Nuzzo JB, Golub JE, Chaulk P, Shah M. Analysis of latent tuberculosis infection treatment adherence among refugees and other patient groups referred to the Baltimore City Health Department TB clinic, February 2009-March 2011. J Immigr Minor Health. 2015; 17:56–65. [PubMed: 23907316]
10. Linton SL, Celentano DD, Kirk GD, Mehta SH. The longitudinal association between homelessness, injection drug use, and injection-related risk behavior among persons with a history of injection drug use in Baltimore, MD. Drug Alcohol Depend. 2013; 132:457–465. [PubMed: 23578590]
11. Keen L 2nd, Khan M, Clifford L, Harrell PT, Latimer WW. Injection and non-injection drug use and infectious disease in Baltimore City: Differences by race. Addict Behav. 2014; 39:1325–1328. [PubMed: 24837755]

12. Hesselink DA, Yoo SM, Verhoeven GT, Brouwers JW, Smit FJ, van Saase JL. A high prevalence of culture-positive extrapulmonary tuberculosis in a large Dutch teaching hospital. Neth J Med. 2003; 61:65–70. [PubMed: 12765226]
13. United States Census Bureau. [cited 2015 Oct 5] State & County QuickFacts. 2015. Available from: http://quickfacts.census.gov/qfd
14. Rieder HL, Snider DE Jr, Cauthen GM. Extrapulmonary tuberculosis in the United States. Am Rev Respir Dis. 1990; 141:347–351. [PubMed: 2301852]
15. Leeds IL1, Magee MJ, Kurbatova EV, del Rio C, Blumberg HM, Leonard MK, et al. Site of extrapulmonary tuberculosis is associated with HIV infection. Clin Infect Dis. 2012; 55:75–81. [PubMed: 22423123]
16. Naing C, Mak JW, Maung M, Wong SF, Kassim AI. Meta-analysis: The association between HIV infection and extrapulmonary tuberculosis. Lung. 2013; 191:27–34. [PubMed: 23180033]
17. Antony SJ, Harrell V, Christie JD, Adams HG, Rumley RL. Clinical differences between pulmonary and extrapulmonary tuberculosis: A 5-year retrospective study. J Natl Med Assoc. 1995; 87:187–192. [PubMed: 7731067]
18. Noertjojo K, Tam CM, Chan SL, Chan-Yeung MM. Extra-pulmonary and pulmonary tuberculosis in Hong Kong. Int J Tuberc Lung Dis. 2002; 6:879–886. [PubMed: 12365574]
19. Pusch T, Pasipanodya JG, Hall RG 2nd, Gumbo T. Therapy duration and long-term outcomes in extra-pulmonary tuberculosis. BMC Infect Dis. 2014; 14 115-2334-14-115.
20. Blumberg HM, Burman WJ, Chaisson RE, Daley CL, Etkind SC, Friedman LN, et al. American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America: Treatment of tuberculosis. Am J Respir Crit Care Med. 2003; 167:603–662. [PubMed: 12588714]

Highlights

- We perform a cohort study of tuberculosis (TB) cases treated at a health department
- We examine clinical differences among extrapulmonary and pulmonary TB patients
- Patients with extrapulmonary TB present with atypical symptoms
- They also and undergo prolonged treatment and experience increased hospitalizations
- Extrapulmonary TB must be further examined to improve diagnosis and treatment

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Table 1

Socio-demographic characteristics of patients[φ]

Characteristic*	Only PTB n=99 (%)	Only EPTB n=46 (%)	EPTB/PTB n=18 (%)	Total n= 163 (%)	*p*-value
Gender					0.996
Male	61 (61.6)	28 (60.9)	11 (61.1)	100 (61.4)	
Female	38 (38.4)	18 (39.1)	7 (38.9)	63 (38.6)	
Origin of birth					0.830
Foreign born[†]	42 (42.4)	22 (47.8)	8 (44.4)	72 (44.2)	
United States born	57 (57.6)	24 (52.2)	10 (55.6)	91 (55.8)	
Age[**]					0.960
0-14	2 (2.0)	2 (4.4)	1 (5.6)	5 (3.1)	
15-24	8 (8.1)	3 (6.5)	2 (11.1)	13 (8.0)	
25-44	38 (38.4)	17 (37.0)	7 (38.9)	62 (38)	
45-64	29 (29.3)	11 (23.9)	5 (27.8)	45 (27.6)	
>65	22 (22.2)	13 (28.3)	3 (16.7)	38 (23.3)	
Ethnic origin					0.467
White	8 (8.1)	5 (10.9)	1 (5.6)	14 (8.6)	
African-American	62 (62.6)	28 (60.9)	12 (66.7)	102 (62.6)	
Hispanic	9 (9.1)	4 (8.7)	4 (22.2)	17 (10.4)	
Asian/Pacific Islander	20 (20.2)	9 (19.5)	1 (5.6)	30 (18.4)	
HIV status					0.182
Positive	11 (11.1)	4 (8.7)	5 (27.8)	20 (12.3)	
Negative	83 (83.8)	38 (82.6)	13 (72.2)	134 (82.2)	
Unknown	5 (5.1)	4 (8.7)	0 (0)	9 (5.5)	

PTB= pulmonary tuberculosis; EPTB = extrapulmonary tuberculosis; EPTB/PTB= extrapulmonary and pulmonary tuberculosis

[φ]Pearson's χ squared tests used to analyze differences in gender, origin, age category, ethnic origin, and HIV status. One-way analysis of variance and student's t-tests used to analyze mean age of presentation by site of TB, HIV status, and origin.

[*]Evaluation of site of TB by year of referral: 2008: 19/33 [57.6%] PTB, 8/33 [24.2%] EPTB, 6/33 [18.2%] EPTB/PTB; 2009: 14/22 [63.6%] PTB, 4/22 [18.2%] EPTB, 4/22 [18.2%] EPTB/PTB; 2010: 22/38 [57.9%] PTB, 13/38 [34.2%] EPTB, 3/38 [7.9%] EPTB/PTB; 2011: 19/29 [65.5%] PTB, 8/29 [27.6%] EPTB, 2/29 [6.9%] EPTB/PTB; 2012: 12/20 [60%] PTB, 6/20 [30%] EPTB, 2/20 [10%] EPTB/PTB; 2013: 13/21 [61.9%] PTB, 7/21 [33.3%] EPTB, 1/21 [4.8%] EPTB/PTB

[†]Countries: Nepal (10), India (8), Kenya (6), Ecuador (5), Philippines (5), Ethiopia (4), Honduras (4), Mexico (4), South Korea (4), Other (22).

** Mean age of presentation 47.3 (SD=20.3). No difference in mean age by site of TB (47.4 [SD=20.2] for PTB only; 48.3 [SD=21.1] for EPTB only; 44 [SD=19.5] for EPTB/PTB; p=0.74) or HIV status (47 [SD=21] for HIV negative; 46 [SD=8] for HIV positive; 50 [SD=29] for unknown HIV status; p=0.85). Foreign born presented at younger mean age than United States born (38 [SD=17.6] vs. 54 [SD=19.3]; p<.001).

Table 2

Clinical characteristics of patients[φ]

Characteristic	Only EPTB n=46 (%)	Some form of PTB n=117(%)	*p*-value
Initial Symptoms [*]			
Cough	14 (30.4)	72 (61.5)	<0.001
Lymphadenopathy	14 (30.4)	8 (6.8)	<0.001
Weight loss	13 (28.3)	56 (47.9)	0.023
Fever	13 (28.3)	43 (36.8)	0.304
Chest pain	7 (15.2)	24 (20.5)	0.438
Anorexia	6 (13.0)	22 (18.8)	0.380
Night sweats	5 (10.9)	46 (39.3)	<0.001
Altered mental status	5 (10.9)	5 (4.3)	0.114
Back pain	3 (6.5)	1 (0.9)	0.035
Shortness of breath	3 (6.5)	5 (4.3)	0.550
Malaise	2 (4.3)	9 (7.7)	0.444
Hemoptysis	1 (2.2)	9 (7.7)	0.186
GI symptoms	5 (10.9)	7 (6.0)	0.282
EPTB disease site [†]			
Lymph Node	14 (30.4)		
Pleural	11 (23.9)		
Bone	9 (19.6)		
CNS TB	7 (15.2)		
GI	4 (8.7)		
Other	1 (2.2)		
Diagnosis [**]			
Microbiologic	32 (69.6)	94 (80.3)	0.126
Pathologic	4 (8.7)	1 (0.9)	0.022
Clinical	10 (21.7)	22 (18.8)	0.672

PTB = pulmonary tuberculosis; EPTB = extrapulmonary tuberculosis; CNS=central nervous system; GI=gastrointestinal

[φ]Pearson's χ squared tests used for all analyses

[*]Analysis of clinical symptoms of some form of EPTB vs. only PTB: some form of EPTB vs. only PTB less likely to have cough (25/64 [39.1%] vs. 61/99 [61.6%]; p=0.005) and hemoptysis (1/64 [1.6%] vs. 9/99 [9%]; p=0.05). Some form of EPTB more likely to have lymphadenopathy than only PTB (18/64 [28.1%] vs. 4/99 [4%]; p<0.001) and GI symptoms (10/64 [15.6%] vs. 2/99 [2%]; p=0.001). No other differences found.

[†]EPTB disease sites for EPTB/PTB were as follows (n): lymph node (6), pleural (6), bone (1), CNS TB (1), GI (1), miliary (3)

[**]More persons with EPTB/PTB had microbiological diagnosis than only PTB or EPTB (17/18 [94.4%] for EPTB/PTB; 77/99 [77.8%] for only PTB; 32/46 [69.6%] for only EPTB), but was not significant (p=0.158). More persons with only EPTB had pathologic diagnosis than only PTB or PTB/EPTB (4/46 [8.7%] for EPTB only; 1/99 for PTB only [1.0%]; 0/18 [0.0%] for EPTB/PTB); was not significant (p=.053). No difference in clinical diagnosis among only PTB, only EPTB, and EPTB/PTB (21/99 [21.2%]; 10/46 [21.7%]; 1/18 [5.6%], respectively; p=.028).

Table 3

Treatment course of patients[φ]

Characteristic	Only PTB n=99 (% or SD)	Some form of EPTB n=64 (% or SD)	*p*-value
Treatment outcome [*]			0.256
Treatment success[†]	81 (89.0)	47 (82.5)	
Death	10 (11.0)	10 (17.5)	
Mean treatment duration in weeks (SD) [**]	31.8 (8.1)	37.9 (11.7)	<0.001
Mean treatment duration in weeks by site EPTB			<0.001
Lymph Node		32.9 (8.5)	
Pleural		32.8 (6.1)	
Bone		50.3 (11.1)	
CNS TB		58.5 (9.2)	
GI		34.7 (10.8)	
Miliary		42 (13)	
Hospitalization at time of diagnosis	48 (48.5)	37 (57.8)	0.244
Subsequent hospitalization [***]	20 (20.2)	25 (39.1)	0.009

PTB= pulmonary tuberculosis; EPTB=extrapulmonary tuberculosis; CNS=central nervous system; GI=gastrointestinal; SD=standard deviation

[φ]Treatment outcome, hospitalization at time of diagnosis, and subsequent hospitalization analyzed using Pearson's χ squared tests. Mean treatment duration by site of TB and treatment outcome by age of presentation analyzed using one-way analysis of variance and student's t-tests.

[*]Outcomes available for 148 patients (7 transferred out, 3 lost to follow up, and 5 still on treatment at time of analysis). More persons with only EPTB had an outcome of death compared to only PTB and EPTB/PTB; was not significant (8/40 [20.0%]; 10/91 [11.0%]; 2/17 [11.8%] for only EPTB, only PTB, and EPTB/PTB, respectively; p=0.371).

[†]Treatment success = alive and cured of TB at end of treatment. Persons who had treatment success were younger than those who did not (mean age 44.7 [SD=19.9] vs. 63.3 [SD=19.2]; p<.001).

[**]Data analyzed on 127 patients (20 patients who died and 1 MDR-TB patient excluded). There was a difference in mean treatment duration comparing those with EPTB only (n=32, mean duration 37.9 weeks) to some form of PTB (n=95, mean duration of 32.8 weeks; p=.012).

[***]Subsequent hospitalization = any hospitalization after treatment was initiated