

ORIGINAL ARTICLE

CLINICAL PROFILE OF EXTRAPULMONARY TUBERCULOSIS CASES ADMITTED AND DIAGNOSED IN A TERTIARY GOVERNMENT HOSPITAL FROM JANUARY 2006 TO JUNE 2010.

AUTHORS: Regie S. Santos, MD
Hospital ng Makati

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CORRESPONDENCE:

Dr. Regie Santos
Email: cotri_redge@yahoo.com

ABSTRACT

Objective: The aim of this study was to determine the prevalence and pattern of Extra-pulmonary Tuberculosis (EPTB) cases that were admitted and diagnosed in a tertiary government hospital from January 2006 to December 2010.

Methodology: Records of pediatric patients who were admitted in a tertiary government hospital from January 2006 to December 2010 with a diagnosis of Extra-pulmonary Tuberculosis were reviewed. The following information was gathered: demographic profile, clinical profile, results of PPD, complications and mortality rate, and laboratory results.

Results: The sixty-six cases constituted 7.8% of the total pediatric admissions during the same period. There was no significant difference as to sex distribution (53% males vs. 47% females, with 1:1 ratio).Majority of cases involved the meninges (72.7%), followed by lymph node (6.1%), liver (6.1%), bone (6.1%) and genitourinary (3.0%). The three most common symptoms were nonspecific: fever, anorexia and weight loss. The occurrence of fever was universal among all admitted cases of Extrapulmonary TB. With regards to prognosis, the majority (83%) of cases were discharged in improved condition. The case fatality rate was 16.7%.

Conclusion: The incidence of new cases of EPTB has remained constant, despite the decline in new cases of active pulmonary TB.

INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by mycobacterium, mainly Mycobacterium TB. It has been present in the human population since antiquity and became a major cause of death and disability in most parts of the world, especially in developing countries. The disease can affect multiple body systems. Although children and persons with immunodeficiencies, such as HIV infection, are at greater risk to have extra-pulmonary TB, pulmonary disease remains the most common type of illness seen worldwide. When the bacteria became active, about 75% of cases are pulmonary TB and the remaining 25% are extra-pulmonary.¹ TB has probably killed 100,000 million people over the past 100 years and has been the world's second leading cause of death among the infectious disease after HIV/AIDS.² According to the WHO estimates, there were 8.8 million new TB cases in 2005 throughout the world, of which 7.4 million (34% of the global incident cases) occurred in Asia and Sub-Saharan Africa. However, the estimated incidence rate in Sub-Saharan Africa is approximately twice that of the South-East Asia Region, at nearly 350 cases per 100,000 population.^{3,4} It is estimated that a total of 1.6 million people died of TB, including 195,000 patients infected with HIV in 2005; it has also been reported that the highest numbers of death (544,000 cases) and the highest mortality per capita (74 cases per 100,000 population) are in the African region.⁴ Although global TB prevalence and death rates have possibly been declining for several years the total number of TB cases was still rising slowly due to continuing growing case-load in Africa, Eastern Mediterranean and South-East Asia Region.³

Extrapulmonary TB (EPTB) is the result of the dissemination of tubercle bacilli from an initial focus in the lungs soon after primary infection.⁵ The dissemination is primarily by way of lympho-

hematogenous route⁶, with seeding of virulent tubercle in almost all of the organs and tissues of the body. Although in most patients, both pulmonary and extrapulmonary lesions, eventually heal clinically subtle granulomas contain tubercle bacilli which can remain viable for decades.⁷ The incidence of new cases of EPTB has remained constant, despite the decline in new cases of active pulmonary TB. This might be due to delay in recognition, and particularly a lack of consideration of TB when the presenting symptoms are not respiratory. EPTB should be considered in the differential diagnosis of bone, joints, genitourinary tract and central nervous system diseases.⁸ The aim of my research was to determine the prevalence and pattern of EPTB cases that were admitted and diagnosed in a tertiary government hospital from January 2006 to December 2010.

METHODOLOGY

Subjects

Patients aged 0-17 years who were admitted from January 2006 to June 2010 with a diagnosis of EPTB were included. Included also in this study were patients with one or more of the following: (1) positive AFB smear from secretion, (2) positive TB culture; (3) with history of exposure to TB; and (4) clinical presentation of the disease with marked improvement after anti-tuberculosis treatment and duration of hospital stay. EPTB was diagnosed based on symptoms and with one or more of the following: (1) positive AFB smear from secretion, (2) positive TB culture (3) with history of exposure to Tuberculosis, and (4) clinical presentation with Tuberculosis with marked improvement after anti-tuberculosis treatment.

Methods

Records of patients diagnosed with Extrapulmonary TB in a tertiary government

hospital from January 2006 to December 2009 were reviewed to determine the number of TB cases and its proportion to pediatric admissions. The following information were gathered: (a) demographic profile which included gender, age, socio-economic status and district from which patient came from; (b) clinical profile which included organ involved, history of exposure, co-morbidities, clinical presentation and symptoms, and results of PPD; complications, mortality rate and laboratory results.

STATISTICAL ANALYSIS:

Data was encoded and tallied using SPSS 14 for Windows. Descriptive statistics were generated for all variables: for nominal data, frequencies and percentages were computed; and for numerical data, mean (95% CI) was generated. A comparison of the different variables under study was done using the T test for continuous variable and chi square-test for nominal variables. Significance was set at 5%. Attributable fraction was computed for variables associated with risks of exposure. Period prevalence was likewise computed for EPTB against pediatric admissions. Case fatality ratio was determined per organ involvement and against all reported cases within the four-and-a-half year time period.

RESULTS

There were 66 EPTB pediatric cases from January 2006 to June 2010 or 7.73% of the total pediatric admissions. The number of admissions due to the disease had been increasing during the four-and-a-half year time period when computed per 10,000 population from the total number of pediatric admission; (Figure 1).

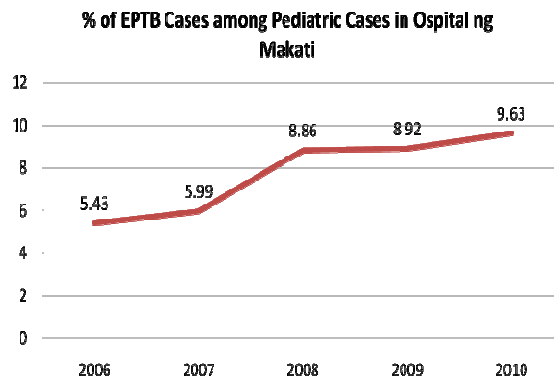


Figure 1: Period Prevalence of Extrapulmonary TB against total Pediatric Admission, January 2006 – June 2010

The proportion of admitted cases due to EPTB to the total number of TB cases had been increasing every year from January 2006 to June 2010, from 1.39%, 3.0%, 4.44%, 5.04% to 5.14%, respectively. While the highest number of cases within that time period was recorded in 2009 [Freq = 19, (5.04%)], the highest relative increase was recorded between 2006 and 2007 (Risk Difference = 1.61). (P values = 0.115, 0.282, 0.738, 1.000). It was also noted that the total number of PTB cases were decreasing while the number of EPTB were gradually increasing during the same period (Table 1).

The highest proportion of admitted cases of EPTB during the study period was among children aged five-to-nine years old followed by children 10 to 17 years old. The average age of admitted cases was 6.9 years old (5.7 – 8.1 years) (Table 2). For the sex differentiation, there was no significant difference (P=0.602) in the distribution; male cases comprised 53%, while female cases comprised 47%, with a male to female ratio of 1:1. The mean age for male cases was higher at 8.5 years) when compared to female cases at 5.1 years. the mean difference was statistically significant (Mean Difference 3.36; P = 0.004).

Table 1. Proportion of Extrapulmonary TB against total (pediatric) TB Admission

Year	EPTB (%)	PTB	Total TB Cases
2006	6 (1.4)	432	438
2007	14 (3)	452	466
2008	18 (4.4)	387	405
2009	19 (5)	358	377
2010	9 (5.1)	166	175
TOTAL	66 (3.54)	1,795	1,861

Table 2. Frequency Distribution of EPTB cases as to age and sex of admitted patients.

Age	Male	Female	Total	%
3 – 11 mos	1	9	10	15.2%
1 – 4 yrs	6	7	13	19.7%
5 – 9 yrs	16	10	26	39.4%
10-17 yrs	12	5	17	25.8%
Total	35 (53.0%)	31 (47.0%)	66	100%

The majority of admitted EPTB cases were residents of Makati (75.8%), the proportion for which were equally distributed to the city's two districts (38% each). On the other hand, 24% of the cases were from outside of the said area. The majority of EPTB cases involved the meninges which comprised 72.7% of total cases. This was followed by lymph node (6.1%), liver (6.1%), bone (6.1%) and genitourinary (3.0%). The least frequencies involved the spleen, heart, peritoneum and ileum, with one case for each (1.5%) (Table 3). There was no admitted patient with more than one extrapulmonary organ site involved. For the majority of EPTB cases (73%)

which exhibited in the meninges, the mean age of cases was 6.2 years. Liver, bone and genitourinary involvement were most seen in children older children > 7 years of age.

(Table 3).

Table 3. Frequency Distribution of EPTB cases as to organ involved.

Organ Involved	Frequency (%)	Mean Age (yrs)
Meninges	48 (72.7)	6.2
Lymph Node	4 (6.1)	5.8
Liver	4 (6.1)	11
Bone	4 (6.1)	7.8
Genitourinary	2 (3.0)	12.5
Ileum	1 (1.5)	
Peritoneum	1 (1.5)	
Heart	1 (1.5)	
Spleen	1 (1.5)	
TOTAL	66 (100)	

Exposure to TB was universal to all EPTB cases. The next higher associated exposure was from cigarette smoking (93.9%), followed by previous history of PTB (74.2%), and lastly, those with comorbidities (68.2%). The proportion of EPTB in the exposed group which can be attributable to a factor (i.e. attributable fraction) was highest among those with exposure to PTB, followed by those with exposure to cigarette smoking, presence of BCG vaccination, history of PTB and presence of co-morbidities (Table 4).

Fifty-four percent of EPTB cases had findings of TB on chest x-ray. Among such cases, majority reported findings of hilar adenopathy (18.2%), followed by military pattern (13.6%), TB Pneumonia (7.6%) and PTB plus pleural effusion (6.1%). For those cases of EPTB with a negative chest x-ray report (46%), 18.2 % was reported normal, 5.2% presented with findings of pneumonia, 6.1% presented with pleural effusion, then findings of atelectasis and pneumothorax presented at 3% each (Table 7). For the PPD skin test, there was a significant

number of cases (P= 0.0001) who tested positive (52 cases or 87.9%), against those who tested negative (8 cases or 12.1%).

Table 4. Frequency Distribution and Association of EPTB cases as to history of exposure.

	With Exposure	No Exposure	Risk Estimate (Attributable Fraction)
TB Exposure	66 (100%)	0	100%
History of PTB	49 (74.2%)	17 (25.8%)	65.2%
Exposure to Cigarette Smoke	62 (93.9%)	4 (6.1%)	93.5%
BCG vaccine	49 (74.2%)	17 (25.8%)	65.2%
Co-morbidities (cerebral palsy, pneumonia)	45 (68.2%)	21 (31.8%)	53.4%

Table 5. Frequency Distribution of EPTB cases as to presenting signs and symptoms.

SIGNS AND SYMPTOMS	Frequency (n = 66)	Percentage
fever	66	100
anorexia	56	84.8
weight loss	53	80.3
cough	46	69.7
seizure	43	65.2
vomiting	41	62.1
night sweats	25	37.9
headache	22	33.3
malaise	22	33.3
hemiparesis	15	22.7
dyspnea	14	21.2
abdominal pain	10	15.2
hemoptysis	9	13.6
back pain	5	7.6
chills	3	4.5
urinary symptoms	3	4.5
pleuritic pain	1	1.5
joint pain	1	1.5
murmur	1	1.5

Table 6. Frequency Distribution of Extrapulmonary Tuberculosis cases as to Chest Xray findings.

Chest Xray Findings	
Hilar adenopathy	12 (18.2%)
Miliary pattern	9 (13.6%)
Tb pneumonia	5 (7.6%)
PTB plus pleural effusion	4 (6.1%)
PTB minimal	3 (4.5%)
Pneumonia	10 (15.2%)
Atelectasis	2 (3%)
Pneumothorax	2 (3%)
Normal	12 (18.2%)

The mean length of hospital stay was 3.11 weeks. Approximately half (50%) of the EPTB cases required a hospital stay of at least four weeks. For the remaining cases, 24% stayed for three weeks, 12% stayed for two weeks, and around 14% stayed for the least amount of hospital days of less than or equal to one week.

With regard to outcome, the majority (83%) of cases were discharged in improved condition. EPTB had a case fatality rate of 16.7%; among those who died, the mean age was 5.9 years in whom four were males (36.4%) and seven were females (63.6%). For meningeal involvement, which exhibited the highest number of cases, it has a mortality rate of 14.6% (Table 7).

DISCUSSION

In my study, EPTB constitutes 7.73% of all cases of TB, while about 15% to 20% was reported by Fanning and 10% by Haegi V.^{9, 10} Accurate data on the incidence of disease is difficult to find except in countries where sufficient national data is available. There is wide variation between series depending on the region studied and the ethnic groups. Study done by Charlett, et. al., in the United Kingdom, the White population present with an extrapulmonary site in 15% of cases but those of Bangladeshi, Pakistani or Indian ethnic origin present with an extrapulmonary site in up to 50% of cases¹¹.

Table 7. Frequency Distribution of Mortalities due to EPTB as to age, sex and organ involvement.

Variables		Expired (n=11)	Improved (n=55)
Mean Age		5.9	7.1
Sex	Male	4	31 (56.4%)
	Female	7 (63.6%)	24 (43.6%)
Organ Involved*	Meninges	7 (14.6%)	41 (85.4%)
	Lymph Node	0	4 (100%)
	Liver	2 (50%)	2 (50%)
	Bone	1 (25%)	3 (75%)
	Genitourinary	0	2 (100%)
	Ileum	0	1 (100%)
	Peritoneum	0	1 (100%)
	Heart	0	1 (100%)
	Spleen	1 (100%)	0

For the sex differentiation, there was no significant difference in the distribution. In the study of ShafiUllah, the overall M:F ratio was 1:2, this finding was in accordance with several other studies.¹² The highest proportion of admitted cases of Extrapulmonary TB was children aged five-to-nine years old. In this study, the majority of EPTB cases involved the meninges. A study by ShafiUllah showed the lymph nodes to be the most common site of EPTB as observed in 66% of cases. Some studies have suggested a variable localization of EPTB in the body. In Hong Kong¹³, the most common site of EPTB was the pleura, followed by the lymph nodes, whereas in one study in USA¹⁴, bones and/or joints were the most common sites. Results of ShafiUllah study are comparable to many other studies,^{15,16-18} which reported highest frequency of lymph node involvement. It is likely that TB organism may have tropism for lymph nodes or that tuberculosis of lymph nodes lead to their enlargement which. Other forms of EPTB may be more difficult to diagnose and many may remain unexplored. A study from England showed that

lymph node involvement was the most common site in the body.¹⁹ A study in Holland showed that the most common sites of EPTB were both pleura and lymph node (17% for each).²⁰ Maltezou and his colleagues found the lymph node was the most common site of EPTB in children and EPTB constituted 9% of all cases with TB.²¹ Lymph node involvement in EPTB was correlated with HIV co-infection, female gender, young age and Asian race.²² In this study, there were no admitted patients with more than one extrapulmonary organ sites involved. Study of Mustafa Kursat et al., found that 1.5% of EPTB patients had multi-organ involvement.²³ During the primary infection of TB, bacteria can spread to all organs in the body. Therefore, EPTB can be observed in different organs at the same time.

The presenting signs and symptoms in this study were similar to those seen in pulmonary TB. This study showed that three of the most common symptoms were nonspecific: fever, anorexia and weight loss. The occurrence of fever was universal among all admitted cases of EPTB in this study. In children with EPTB, night sweats, malaise and hemoptysis were not frequently reported.

Eighty percent of Extrapulmonary TB cases had findings of TB on chest x-ray. Hussen et al in 1971 showed that 40 patients out of 367 cases with normal chest x-ray but were suspected clinically to have active PTB gave positive sputum cultures.¹⁷ All patients in this study had no TB culture, since the institution did not have this laboratory test. Majority (87.9%) of the patients had positive PPD test, while 12.1% were negative.

CONCLUSIONS

This study was undertaken to present the clinical features of EPTB with a view of increasing awareness on its existence in order to facilitate

its early treatment and thus decrease morbidity and mortality. The incidence of new cases of EPTB has remained constant, despite the decline in new cases of active pulmonary TB. This might be due to delay in recognition, and particularly a lack of consideration of TB when the presenting symptoms are other than respiratory. EPTB should be considered in the differential diagnosis of bone, joints, genitourinary tract and central nervous system diseases.

RECOMMENDATION

A more comprehensive study, integrating all methods of diagnosis, is needed to determine the exact occurrence of EPTB in our population. All physicians must have a high index of suspicion to diagnose extrapulmonary tuberculosis, as it can resemble any disease in any organ system. Immediate therapy, sometimes even before a definite diagnosis can be made, may be lifesaving.

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