Epidemiology of Extrapulmonary and Disseminated Tuberculosis in a Tertiary Care Center in Oman

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Abstract

Background: The incidence of extrapulmonary and disseminated tuberculosis (TB) cases is increasing worldwide, and this growth significantly impacts TB-related morbidity and mortality. Little is known about the host risk factors for extrapulmonary and disseminated TB. In this study, we examined those risk factors. Materials and Methods: We conducted a retrospective review of all TB cases admitted to Sultan Qaboos University Hospital from 2006 to 2015. We compared extrapulmonary TB (EPTB) cases with pulmonary and disseminated TB cases. We evaluated the risk factors associated with the development of extrapulmonary and disseminated TB using logistic regression analysis. Results: We reviewed 260 TB cases, of which EPTB comprised 37%, PTB comprised 53%, and disseminated TB comprised 10%. The most common sites of infection in the EPTB group were the lymph nodes and the abdomen. Disseminated TB and TB meningitis were more common in expatriates than in Omanis. Patients with EPTB were less likely to smoke compared to a patient with PTB. Patients with disseminated TB had a higher mortality when compared to patients with EPTB (adjusted odds ratio [OR], 0.004; 95% confidence intervals [CI]: 0.001–0.054; \( P = 0.001 \)) and PTB (adjusted OR, 0.022; 95% CI: 0.004–0.115; \( P = 0.001 \)). Human immunodeficiency virus (HIV) was the main risk factor for patients with disseminated TB when compared to patients with extrapulmonary and PTB. Conclusion: The rates of extrapulmonary and disseminated TB in Oman are higher than what has been recognized. Expatriates, patients with HIV, and smokers are at high risk for disseminated TB. In these patients, suspected extrapulmonary sites should be evaluated and sampled to exclude disseminated TB.

Keywords: Disseminated, epidemiology, extrapulmonary, Oman, predictors, tuberculosis

Introduction

Tuberculosis (TB) remains a major threat to humanity despite improvements in health-care systems and the widespread implementation of TB control programs. In 2015, the World Health Organization (WHO) estimated 10.4 million individuals had TB, but only 6 million cases had been reported to the WHO.\(^1\) Alarming, this means that more than half of all TB cases are unrecognized or unreported to the WHO. TB involving an organ other than the lung is known as extrapulmonary TB (EPTB). EPTB is one of the major reasons for underdiagnosis. TB is curable if recognized early and appropriately treated. However, the worldwide incidence of EPTB and disseminated TB cases (cases where pulmonary and EPTB are found in the same patient) are increasing and significantly contributing to TB-related morbidity and mortality.\(^2\)

While studies have suggested that EPTB and disseminated TB are common in immunocompromised patients,\(^3\) other risks factors are still unknown. Few studies of extrapulmonary and disseminated TB have been published recently, particularly in the Middle East and Gulf area population which significantly contribute to the global burden of TB.\(^4\)

In this retrospective study, we reviewed all TB cases admitted to a tertiary care center in Oman over a 10-year period from 2006 to 2015. We compared the demographics and clinical characteristics of extrapulmonary, pulmonary, and disseminated TB cases. The aim of this study is to enhance the understanding of the epidemiology of EPTB and disseminated TB by exploring the risk factors and common clinical presentations. These findings should improve the early detection of EPTB and disseminated TB cases.

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We retrospectively reviewed TB cases seen at Sultan Qaboos University Hospital from August 2006 to December 2015. We included both *Mycobacterium* TB culture-positive and culture-negative cases. Culture-negative cases were included if they had clinical and histological findings suggestive of TB. We did not exclude any age groups. All data were gathered from the hospital’s electronic medical records.

We used the WHO classification to categorize TB cases. PTB cases were composed of cases where the infection involved the lung parenchyma or the tracheobronchial tree. TB infections involving any other organs or intrathoracic lymph nodes or tuberculous pleural effusion without radiographic abnormalities in the lungs comprised cases of EPTB.[1] Patients with both PTB and EPTB were classified as cases of disseminated TB. All 3 groups were compared to each other. Variables collected were age, sex, country of origin, living area, previous treatment for TB, immunosuppressive therapy, smoking, alcohol or drug use, and underlying clinical diseases such as chronic renal disease, chronic liver disease, malignancy, and human immunodeficiency virus (HIV). Immunosuppressive therapy was defined as receiving cytotoxic agents or corticosteroids for any period before the diagnosis of TB. Diabetes mellitus (DM) diagnosis was determined by documented history of DM. Any death before or during TB treatment was considered TB-related mortality.

Descriptive statistics were used to describe the data. We reported categorical variables using frequency and percentage, and we compared them using Chi-square test (or Fisher exact test when applicable). For normal distributed continuous variables, we used mean and standard deviation to present the data while analysis was performed using Student’s t-tests. For nonnormal distributed continuous variables, median and interquartile range were used to summarize the data and analysis performed using Wilcoxon–Mann–Whitney tests.

We evaluated the risk factors associated with the development of EPTB and disseminated TB by using Logistic regression model utilizing the backward stepwise selection procedure with a significance level of >0.2 for the removal from the model. *P* < 0.05 was considered statistically significant. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated to compare groups. StataCorp. 2011. Stata Statistical Software: Release 12. (StataCorp LP, College Station, TX, USA) was used for data analysis. This study was approved by the institutional review board of Sultan Qaboos University.

### Results

We reviewed a total of 260 TB cases; the mean age was 41 ± 20 years, and males represented 60% of all TB cases. Omani comprised 90% of the cases, and 196 cases (75%) were TB-culture confirmed cases [Table 1]. There were 20 cases (7.7%) of HIV and 29 cases (15.4%) of DM. Death occurred in 36 TB cases (13.9%). Cancer diagnosis was found in 12 cases (16.7%) while 19 cases (7.3%) had been previously diagnosed with TB. EPTB, PTB, and disseminated TB cases represented 37%, 53%, and 10% of the total cases, respectively. The most common sites of infection in the EPTB group were the lymph nodes (42%), the abdomen (31%), brain (10%), musculoskeletal tissue (10%), and other sites (7%). Our subgroup analysis revealed TB meningitis was more common in expatriates than in Omani (OR: 11.5; 95% CI: 3.069–43.098; *P* = 0.001).

Comparing EPTB with PTB cases, our unadjusted analysis [Table 2] revealed EPTB cases were more associated with female gender (unadjusted OR: 2.15; 95% CI: 1.259–3.670; *P* = 0.005), nonsmokers (OR: 0.246; 95% CI: 0.108–0.556; *P* = 0.001), lower mortality (OR: 0.262; 95% CI: 0.073–0.933; *P* = 0.028), and negative TB cultures (OR: 0.362; 95% CI: 0.193–0.679; *P* = 0.001). However, after adjusting for confounders in the multivariable logistic model, the only variables that remained significant were the smoking status (adjusted OR: 0.318; 95% CI: 0.131–0.770; *P* = 0.011) and negative TB culture (adjusted OR: 0.443; 95% CI: 0.229–0.858; *P* = 0.016).

Table 3 shows our comparison of EPTB cases with disseminated TB. In our adjusted analysis, EPTB cases were less likely to be expatriates (adjusted OR: 0.078; 95% CI: 0.012–0.497; *P* = 0.007), less likely to be smokers (adjusted OR: 0.106; 95% CI: 0.011–0.962; *P* = 0.046), less likely to be HIV positive (adjusted OR: 0.047; 95% CI: 0.005–0.461; *P* = 0.009), and they had lower TB-related mortality (adjusted OR, 0.004; 95% CI: 0.001–0.054; *P* = 0.0001). Moreover, EPTB cases were more likely to have a culture positive than disseminated TB cases (adjusted OR: 6.348; 95% CI: 1.153–34.939; *P* = 0.034). In our unadjusted analysis, we found EPTB associated more with the female gender, but this association became insignificant in the adjusted analysis.

When we compared PTB with disseminated TB [Table 4], we found PTB cases were more likely to be culture positive (adjusted OR: 6.720; 95% CI: 1.698–26.599; *P* = 0.007). However, they were less likely to be expatriates (adjusted OR: 0.069; 95% CI: 0.013–0.359; *P* = 0.001), HIV positive (adjusted OR: 0.171; 95% CI: 0.036–0.822; *P* = 0.027) and had lower TB-related mortality (adjusted OR: 0.022; 95% CI: 0.004–0.115; *P* = 0.0001). Smoking, as a variable, was not associated with PTB when compare with disseminated TB.

### Discussion

Our study revealed higher rates of EPTB and disseminated TB compared to the rates estimated by the WHO in both Oman and other Gulf countries.[1,6] This difference in the rates may be due to underreporting of TB cases to the national TB programs and WHO. Nevertheless, the rates reported in hospital-based TB studies are often more accurate than those reported by national surveillance TB programs. Our finding that lymph nodes and the abdomen were main sites for EPTB aligned with many other studies reporting the same.[7,8]
Our data suggest that disseminated and TB meningitis were both more in expatriates than in Omani. This could be due to the protective effect of the Bacillus Calmette–Guérin (BCG) vaccine common among Omanis. The BCG vaccine is known to decrease the risk of disseminated and TB meningitis when administered early in life,[9,10] and the BCG vaccination program in Oman is more well-established compared to the countries of origin of the expatriates in Oman. It may also be that the routine screening of expatriates for PTB on entry to the country may increase the number of EPTB cases relative to PTB cases.

The rate of HIV and TB coinfection was similar to the rates in other developed countries.[2] We found no significant
The rates of extrapulmonary and disseminated TB in Oman are higher than what has been recognized. Expatriates, patients with HIV, and smokers are at high risk for disseminated TB. In these patients, suspected extrapulmonary sites should be evaluated and sampled to exclude disseminated TB. Further studies are needed to identify the role of mycobacterial virulence factors and other host risk factors in the pathogenesis of disseminated and EPTB.

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Conflicts of interest
There are no conflicts of interest.

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