TUBERCULOSIS AND MDR-TB IN THE NORTHERN EMIRATES OF UNITED ARAB EMIRATES: A 5-YEAR STUDY

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Abstract. In this study, we describe the prevalence of TB and occurrence of multi-drug-resistance tuberculosis (MDR-TB) in a major referral hospital belonging to the Ministry of Health in Sharjah, United Arab Emirates (UAE). A retrospective review of the clinical and laboratory records of 1,810 suspected cases of TB was carried out between January 2004 and September 2008. The antimicrobial susceptibility patterns of each *Mycobacterium tuberculosis* isolate were analyzed. During the study period, 312 *M. tuberculosis* culture confirmed cases were recorded; 230 were males and 82 were females. The majority of TB cases (36%) were seen among expatriates from South and Southeast Asian countries. Fifty-one active TB cases (16%) were reported in native people (Emaratis) of the country. The peak age group was between 16 and 45 years. Among first-line antituberculosis drugs, resistance to isoniazid was the most common (21%), followed by streptomycin (14%). MDR-TB was found in 15 cases (4.8%)**.** Although the prevalence of TB in UAE is fairly low, an increasing number of cultures confirmed TB and MDR-TB among native and expatriate patients, necessitating improved vigilance in case detection, effective management and prevention of MDR and XDR-TB emergence in the country.

Key words: MDR-TB, *M. tuberculosis*, United Arab Emirates.

INTRODUCTION

Tuberculosis is one of the most important infectious diseases worldwide with 9.2 million new cases added each year (WHO, 2006; Zager and McNerney, 2008). United Arab Emirates (UAE) having a population of four and a half million people (WHO, 2008c), has a low-incidence of TB, with an annual incidence rate of 16 cases/ 100,000 population (WHO, 2006). The country's population is constituted of a large number of expatriates (approximately 80%), many of whom are from countries like India, Pakistan, Sri Lanka, Indonesia and the Philippines, where TB is endemic. Despite effective screening, it is expected that new immigrants will added to the burden of TB disease in the country because of reactivation of latent

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infection (Talbot *et al*, 2000; Lobato *et al*, 2008). Many of these immigrants may be carrying MDR-TB strains that can be transmitted in the local community (Talbot *et al*, 2000; Moniruzzaman *et al*, 2006). The present study describes the prevalence of TB and the occurrence of MDR-TB at a Ministry of Health referral hospital in Sharjah, United Arab Emirates.

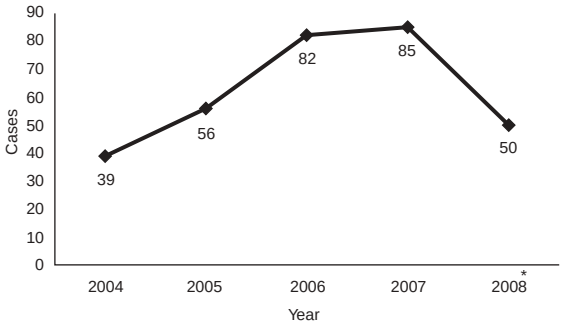
MATERIALS AND METHODS

The UAE consists of seven states, termed emirates. Six of these, namely Dubai, Sharjah, Ajman, Umm al-Quwain, Ras al-Khaimah and Fujairah are considered Northern emirates, due to their geographical location. In Sharjah, Al Qassimi Hospital is the referral center for the diagnosis and management of TB. The hospital receives clinically suspected cases of TB referred from a large number of primary health centers and twelve other hospitals located within the neighboring Northern emirates. Tuberculosis is a notifiable disease in the UAE, and the Ministry of Health uses a case definition of TB based on the site or location of the disease, x-ray findings and bacteriological reports from both smears and cultures (Ministry of Health, UAE, 2006). However, a definite diagnosis of TB disease depends on a positive culture for *M. tuberculosis*. For consistency in our results we agreed "a positive culture for *M. tuberculosis* confirms the diagnosis of TB disease". A culture was perfromed on all specimens, regardless of the AFB smear results (Dam and Bose, 2000).

We reviewed the clinical and laboratory records of 1,810 patients referred by clinicians as suspected cases of tuberculosis based on their presenting symptoms, clinical findings and x-ray reports between January 2004 and September 2008. Basic patient demographic information including age, gender, nationality, and clinical information, such as underlying condition, immune status, treatment and outcome, were recorded. From a laboratory diagnosis of mycobacterial infection perspective, information regarding the clinical specimen received, Ziehl-Neelsen stain reports, specimen processing, culture and identification of mycobacteria isolates using BACTEC™ MGIT™ 960 (Becton Dickinson Diagnostic Systems, Sparks, Maryland, USA), and drug susceptibility patterns of *M. tuberculosis* isolates were analysed. Drug susceptibility testing of *M. tuberculosis* isolates to streptomycin (STR), isoniazid (INH), rifampin (RIF), and ethambutol (EMB) was performed using the BACTEC™ MGIT™ 960 SIRE Kit **(**Becton Dickinson Diagnostic Systems, Sparks, Maryland, USA). Susceptibility test against pyrazinamide (PZA) at a concentration of 100 μg/ml was performed using the BACTEC MGIT 960 PZA kit from the same source (Butler *et al*, 1982). Strains showing resistance to isoniazid and rifampin, with or without resistance to other drugs, were defined as MDR-TB (Moore *et al*, 1997).

RESULTS

Of the 1,810 cases of suspected tuberculosis in which smear examination and/or culture were carried out, the culture confirmed *M. tuberculosis* disease in 312 cases. Among these 312 culture confirmed TB cases, 230 (74%) were males and 82 (26%) were females. The mean age of the TB patients was 36 years and the age group between 16 and 45 years had the highest rate of TB disease (68%). The majority of TB cases (51%) were seen among expatriates from five South and Southeast Asian countries: India, Indonesia, Pakistan, the Philippines, and Sri Lanka. Fifty-one



* until September 2008

Fig 1–Annual distribution of culture confirmed TB cases between January 2004 and September 2008.

active TB cases (16%) were reported among the native residents of the country. In 63 (20%) culture confirmed TB cases, information regarding the nationality of the patient was not available. Sputum was the most common clinical specimen obtained for laboratory investigation of TB (78%). During the study period, only one TB patient had documented human immunodeficiency virus (HIV) positive serology. There was only one death due to TB disease reported in a 25 year old female patient who was resistant to all first line antituberculosis drugs.

In the 312 culture confirmed cases of TB, 218 (70%) sputum specimens were positive for acid-fast bacilli by microscopy using Ziehl-Neelsen staining. *In vitro* drug susceptibility testing was performed on *M. tuberculosis* isolates from all 312 cases. Resistance to isoniazid, with or without resistance to other first line antituberculosis drugs, was reported in 66 (21%) of 312 specimens. This was followed by resistance to streptomycin, rifampicin and ethambutol in 12, 4 and 9%, respectively. Multidrug-resistance TB was observed in 15 isolates (4.8%), of which 2 were native Emaratis.

DISCUSSION

Between the years 2004 and 2007, a total of 312 bacteriological confirmed cases of TB were reported. The majority of these TB cases were seen among expatriates and especially from Southeast Asian countries, which constitute the leading labor market force in UAE. Although UAE, like many other developed countries, has a successful screening program in the form of mandatory medical examinations to detect TB among immigrants and prevent them from entering into the country, these programs may not be able to detect latent TB cases which may reactivate years later, increasing the risk of transmission in the local community (Rivest *et al*, 1998; Lillebaek *et al*, 2001). During the study period, 51 cases of active TB were detected amongst the native Emaratis population. Although the number appears to be small, it is of great public health consequence taking into consideration the native population of UAE has not been exposed to *M. tuberculosis* infection and may not have immunity against the disease. In our study, the majority of TB cases were males (70%), in the age group between 16 and 45 years, and in the expatriate population of South and Southeast Asian countries. This is in line with the immigrant labor market in the country which is adult male dominated, mostly hailing from countries such as India, Pakistan, the Philippines, Indonesia and Sri Lanka. Several studies have reported similar findings about adult predominance in TB cases among immigrant population in tuberculosis low-incidence countries (Lillebaek *et al*, 2001; LoBue *et al*, 2004).

In the present study, the sensitivity of smear examination using Ziehl-Neelsen stain was reported to be 70%. Although microscopy is a simple, cheap and rapid

diagnostic method for tuberculosis, visualization of acid-fast bacilli in clinical specimens is considered only presumptive evidence of TB (Levy *et al*, 1989; Yilmaz *et al*, 2008). The gold standard for the diagnosis of TB is still a positive culture for *M. tuberculosis* (Lu *et al*, 2000). Culture identification of isolates, and their drug susceptibility tests were performed using a mycobacteria growth indicator tube (MGIT) system which is rapid and has been reported to be having better sensitivity for recovery of mycobacteria from clinical specimens (Levidiotou *et al*, 1999; Macondo *et al*, 2000). Drug resistance is an important concern for TB control programs. In UAE, there has been limited information concerning the incidence of MDR-TB to date, and no systematic studies have been conducted on the subject. None of the 312 culture confirmed cases in our study had received antituberculosis treatment previously. Hence, these were considered as new cases of tuberculosis. However, the finding that 35% of isolates had initial resistance to at least one first-line antituberculosis drug clearly demonstrates drug resistant strains are most likely being imported and circulated in the community. This increases the likelihood of local residents, especially native Emaratis, of being infected by a resistant strain, which is of great concern for both treatment and control of TB. During the study period, we found 15 cases of MDR-TB (3.8%), which is well within the worldwild average of around 5% for MDR-TB (Gonlugur *et al*, 2007)**.** However, it is below the documented resistance rate of 8.5% recorded in the Al Ain medical district of UAE during the year 1999-2000 (Dissanayake *et al*, 2001).

In order to identify the source of TB infection, study the patterns of transmission and molecular epidemiology and drug resistance patterns, molecular techniques such as DNA fingerprints (Glynn *et al*, 1999) and spoligotyping (Bauer *et al*, 1999) have proved to be useful. Such techniques are helpful, especially in a country like UAE, which continues to be a low-incidence country for TB (WHO, 2008b), and has a continuous surge in immigrants, especially from TB endemic countries (Al-Hajoj *et al*, 2007). In a recent study in UAE, the genotypic diversity of isoniazid-resistant *M. tuberculosis* isolates, mostly recovered from expatriate patients, indicated that most expatriates were infected with a unique strain. This strain was imported most likely from their country of origin and their latent infection reactivated in UAE (Ahmad and Fares, 2005). Cases of extensively drug-resistance tuberculosis (XDR-TB) with additional resistance to fluoroquinolones and aminoglycosides are emerging throughout the world (Mitnick *et al*, 2008). However, there have been no such reports from UAE, which may be due to the fact that there is no proper equipment available in the country to verify this problem.

The study had several potential limitations. Firstly, this is a retrospective study analyzing only notified cases of tuberculosis, thus it may not reflect the true incidence of TB in the community. Secondly, as per the regulations of the Ministry of Health, UAE, when an expatriate is diagnosed with having tuberculosis using investigations such as x-rays, AFB smears and/or cultures, he is treated with an intensive course of antituberculosis drugs and examined for 3 successive negative smears. Following this he is sent back to his country of origin with the rest of the drugs to finish his treatment course. This may contribute to under-reporting of TB cases because tuberculosis in expatriates leads to deportation from the country, loss

of a job, disruption of families and other fallouts which might lure them to seek alternative means of being diagnosed and treated. Lastly, it was our inability to follow up the cases and record treatment outcomes, since most cases were expatriates who were obliged to go back to their country of origin after being given the diagnosis of tuberculosis.

In conclusion, an increasing number of culture confirmed TB and MDR-TB cases among native and expatriate populations requires not only effective screening strategies but also preparing laboratories in the country to detect new cases, especially of emerging MDR and XDR-TB and provide satisfactory management in order to eliminate TB from the country (Al-Maniri *et al*, 2007).

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