

TUBERCULOSIS : AN EIGHT YEAR (2000-2007) RETROSPECTIVE STUDY AT THE UNIVERSITY OF MALAYA MEDICAL CENTRE (UMMC), KUALA LUMPUR, MALAYSIA

CA Jetan, I Jamaiah, M Rohela and V Nissapatorn

Department of Parasitology, Faculty of Medicine, University of Malaya,
Kuala Lumpur, Malaysia

Abstract. This was an eight year (2000-2007) retrospective study of tuberculosis in patients admitted to the UMMC. A total of 131 cases were analyzed. Malays constituted the most cases, (43%), followed by Chinese (22%), Indians (17%) and others (18%). The majority of cases were within the 21-60 year old age group, which constituted 69.5% of the total. Males were more commonly affected (65%). Most cases were reported among Malaysians (83%). The majority of patients were unemployed (39%), followed by housewives (10%), laborers (9%), students (8%), shop assistants (7%), and other occupations (27%). The most common presenting complaints were prolonged productive cough, night sweats, fever, anorexia, weight loss (57%), hemoptysis (34%), and undifferentiated symptoms, such as prolonged diarrhea and dysphagia (9%). Sputum was positive for acid-fast bacilli (AFB) in 89%, but only 69% of cases had abnormal chest radiographs. The majority of patients (65%) developed no complications. The most common complications were pleural effusion, pneumothorax and pulmonary fibrosis. The majority of patients (82%) suffered either from diabetes mellitus, hypertension, ischemic heart disease or all 3 conditions. Regarding risk factors for tuberculosis, two were HIV positive and two were intravenous drug users. The majority of the patients (85%) did not complain of any side effects from their anti-tuberculosis treatment. Among those who did complain of side effects, the most common were nausea and vomiting (41%), drug induced hepatitis (37%), blurring of vision (11%) and skin rashes (11%). Two cases of death were reported.

Key words: tuberculosis, retrospective study, Malaysia

INTRODUCTION

Tuberculosis (TB) is caused by bacteria belonging to the *Mycobacterium tuberculosis* complex. The disease usually affects

the lungs, although in up to one third of cases other organs are also involved. In 1995, it was estimated 8.8 million cases of TB occurred worldwide, 95% (5.5 million) of them in developing countries of Asia, Africa (1.5 million), the Middle East (745,000) and Latin America (600,000). It is also estimated that nearly 3 million deaths from TB occurred in 1995, 98% of them in developing countries. In 1995 in the United States, 22,813 cases of TB (8.7

Correspondence: Prof Dr Jamaiah Ibrahim,
Department of Parasitology, Faculty of Medicine,
University of Malaya, 50603 Kuala Lumpur,
Malaysia.

Tel: 603-79674752; Fax: 603-79674754

E-mail: jamaiah@ummc.edu.my

cases per 100,000 population) were reported to the Centers for Disease Control and prevention. A number of factors have been implicated in the increasing rates of TB in the United States, most notably infection due to human immunodeficiency virus (HIV), immigration from countries with a high prevalence of TB, and social problems, such as poverty, homelessness and drug abuse. TB is an important opportunistic disease among HIV-infected persons. In developing countries of Africa, Southeast Asia and Latin America, an estimated 8.5 million people were co-infected with TB and HIV as of the middle of 1996 (Raviglione and O'Brien, 1998).

In the early 1940s and 1950s, TB was the number one cause of death in Malaysia. Patients with TB were admitted to the many sanatoria in various parts of the country and were often managed by surgical means. TB chemotherapy became available only in the late 1950s. Realizing its seriousness, the Malaysian government launched its National TB Control Program (NTP) in 1961. In the year 2000, a total of 15,057 cases of all forms of TB were reported to the government. The incidence rate per 100,000 population was 64.7. Of these, 8,154 (54.2%) were smear positive; the incidence of smear positive cases was 34.7 per 100,000 population. The state with the highest disease burden is Sabah, followed by Wilayah Persekutuan Kuala Lumpur, Sarawak and Pulau Pinang, respectively. Twenty-nine percent, or about one-third of the national TB cases, were from Sabah (Dony *et al*, 2004). In terms of age distribution, the majority of cases were in the 15-54 year old age group. HIV infection is the single most important risk factor for the development of active TB. About 10% of TB cases reported in Malaysia are among the immigrant population.

These are usually immigrant workers from high TB burden neighboring countries. In regard to type of TB, pulmonary TB constitutes 91% of total cases. The most common forms of extra-pulmonary TB seen in Malaysia are TB lymphadenitis, bone and joint TB and miliary TB. Treatment consists of a 6 month regimen using streptomycin or ethambutol in combination with INH, rifampicin and pyrazinamide for 2 months followed by rifampicin and INH biweekly for an additional 4 months. For the year 2000 in Malaysia, smear-positive cases were detected in 70% and the cure rate was 77.6% (Iyawoo, 2004).

TB was the second most common notifiable communicable disease in Malaysia in 2001.

TB remains a common disease in Malaysia, and people should learn to recognize the symptoms for early diagnosis and treatment. The influx of immigrants into Malaysia has made it difficult for the government to control the disease. HIV-positive people are at risk for TB infection because of their depressed immune status. TB is the leading cause of death for people who are living with HIV/AIDS.

The aim of this retrospective study was to identify the cases of TB admitted to the UMMC, their clinical presentations, complications, management and epidemiology.

MATERIALS AND METHODS

The medical records of all the tuberculosis cases admitted to the UMMC, Kuala Lumpur, Malaysia, during the years 2000-2007 (eight years) were analyzed. One hundred and thirty-one medical records of patients with the diagnosis of TB were evaluated. Data analysis was conducted using the program SPSS (Version 13).

RESULTS

Fig 1 shows a steady increase in the number of admissions during 2000-2004, the highest being in 2004 (41 cases) followed by 2006 (29 cases).

Fig 2 shows the most common age group infected was 21-40 years old ($n=49$; 37%), followed by the 41-60 year old age group ($n=42$; 32%). The age group with the fewest cases was age 0-20 years old ($n=4$; 3%). The 21-60 year old age group constituted the majority of cases ($n=91$; 69.5%). More cases were reported among males ($n=85$; 65%) than females ($n=46$; 35%). The majority of cases ($n=110$; 84%) denied any history of contact with TB patients; 21 (16%) reported a history of TB contacts.

Fig 3 shows most cases occurred among Malays (56 cases; 43%), followed by the Chinese (29 cases; 22%), Indians (22 cases; 17%) and others (18%). Most cases ($n=109$; 83%) occurred among Malaysians. Twenty-two cases (17%) were recorded among Indonesians and Myanmar people.

In terms of occupation, the majority of patients were unemployed ($n=51$; 39%), followed by housewives ($n=13$; 10%), laborers ($n=12$; 9%), students ($n=10$; 8%) shop assistants ($n=9$; 7%) and other occupations (cleaners, drivers, factory workers, etc) (27%).

The most common presenting complaints were the typical classical features of prolonged productive cough, night sweats, fever, anorexia and weight loss (57%); 34% presented with hemoptysis and 9% presented with undifferentiated symptoms, such as prolonged diarrhea, dysphagia and anal discharge.

The majority of patients (89%) had a positive sputum for AFB (acid-fast bacilli), but only $n=90$ (69%) had an abnormal chest radiograph; 41 (31%) had a normal

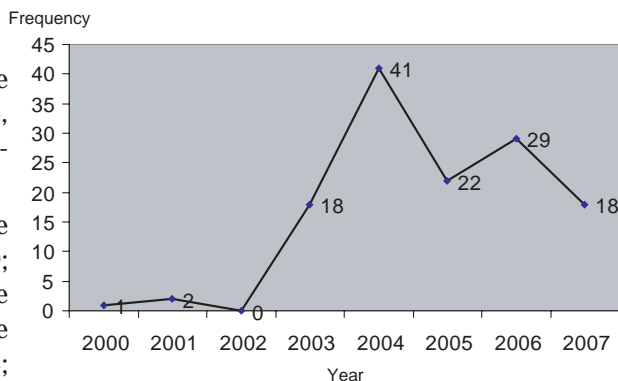


Fig 1-Number of tuberculosis admissions to the UMMC by year (2000-2007).

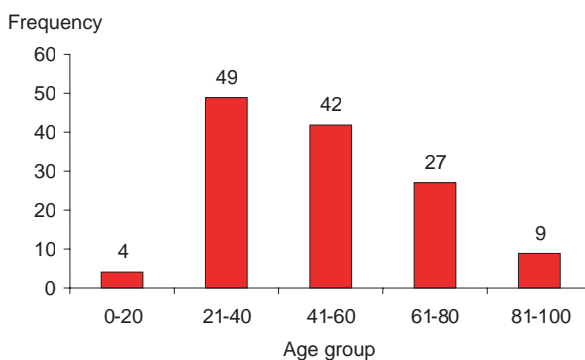


Fig 2-Number of tuberculosis admissions to the UMMC by age group (2000-2007).

chest radiograph.

Fig 4 shows the majority of cases (65%) did not develop any complications. Thirty-two percent ($n=42$) developed respiratory complications, such as pleural effusion, pneumothorax or pulmonary fibrosis. Two percent ($n=3$) developed complications of the central nervous system, such as TB meningitis. One percent ($n=1$) developed ileocecal TB. The greatest number of patients with complications occurred in the 21-40 year old age group, followed by the 41-60 year old age group.

TUBERCULOSIS IN MALAYSIA

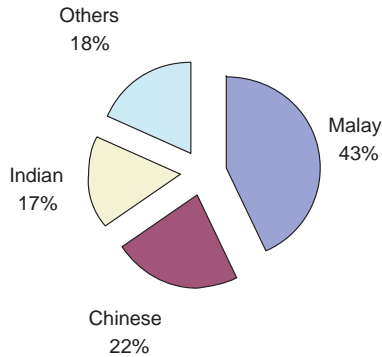
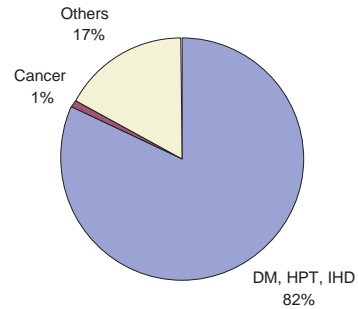
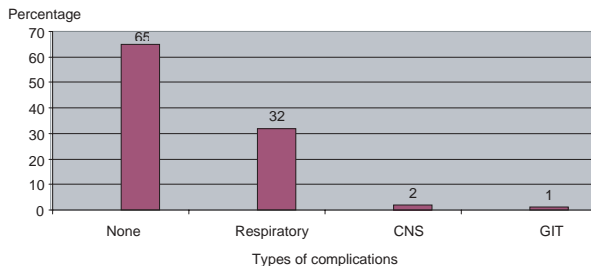


Fig 3-Percentage of tuberculosis admissions to the UMMC by race (2000-2007).



DM, diabetes mellitus; HPT, hypertension; IHD, ischemic heart disease

Fig 5-Types of chronic illnesses in patients with tuberculosis.



CNS, central nervous system; GIT, gastrointestinal

Fig 4-Types of complications developed in patients with tuberculosis.

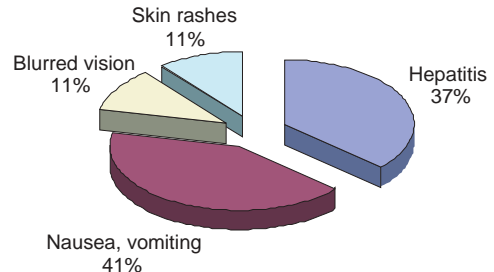


Fig 6-Side effects of anti-tuberculosis treatment.

Fig 5 shows the types of illnesses suffered by patients with tuberculosis. The majority (82%) suffered from diabetes mellitus (DM), hypertension (HPT), ischemic heart disease (IHD) or all 3 conditions. Seventeen percent had SLE, a renal transplant, congenital heart disease or chronic obstructive airway disease and 1% had cancer.

Fig 6 shows the percentage of patients who developed side effects due to anti-TB drugs. Eighty-five percent had no complications related to anti-TB drugs. Of the 15% of patients who developed complications, 41% ($n=8$) experienced nausea and

vomiting during the course of treatment, 37% ($n=7$) developed drug induced hepatitis, 11% experienced blurring of vision and 11% experienced other side effects, such as skin rashes or pruritis.

DISCUSSION

There was a steady increase in the number of admissions from 2000 to 2004, but this declined before increasing again in 2006. The year 2004 had the highest number of admissions with 41 cases followed by 2006 with 29 cases. This increase in TB cases in Malaysia is a cause for worry because it is a disease which is prevent-

able by vaccine. This increasing trend could be due to the massive influx of foreign workers into Malaysia who harbor the infective agent. Another reason could be rapid urbanization and crowding, which leads to various sanitation and health problems. A dirty environment and malnutrition can both make a person more susceptible to TB infection. The larger number of admissions could also be due to increased awareness of TB among patients and their health seeking behavior. Improvements in the health care system may also have contributed to the higher number of detected cases and hospital admissions.

The majority of cases (69.5%) were in the 21-60 year old age group. In this age group, 49 cases (54%) were in the 21-40 year old age group. This is also true in most other studies done regarding the prevalence of tuberculosis in Malaysia. Hayati *et al* (1993) and Nissapatorn *et al* (2003, 2004, 2006a,b) reported similar findings. The reason for this could be the patients who were working were exposed to infections from their work environment. Infection in this age group can have an impact on the country's economy, since this age group is productive and contributes the most to the economy.

Most of the cases occurred among Malaysian citizens (83%), males (65%) and in the Malay ethnic group (43%). Mohamad and Naing (2004) and Nissapatorn *et al* (2006a) reported similar findings. Immigrants made up 17% of the patients (Indonesians and Myanmar people). Although this percentage is small compared to the number of Malaysian patients, it is still a worrying issue. The reason could be due to a higher influx of immigrants recently. Unscreened foreign workers may harbor infective agents, including hepatitis B virus and *Mycobacterium tuberculosis*.

rium tuberculosis. They may easily transmit these infections to others.

Most patients were unemployed (39%), followed by housewives (10%), laborers (9%), students (8%) and shop assistants (7%). Nissapatorn *et al* (2003, 2004, 2006a,b) also reported that most of the cases were among the unemployed. This finding goes against the theory that those who work are more likely to be exposed at their work place. A crowded house with inadequate basic necessities, such as a clean water supply, electricity and sewage disposal, in combination with poor nutrition, could all contribute to susceptibility to infection. Most laborers live in a "rumah kongsi" (shared house) with at least 10 other people in unsatisfactory conditions.

The most common presenting complaints were prolonged productive cough, night sweats, fever, anorexia and weight loss (57%) and hemoptysis (34%), while 9% presented with nonspecific symptoms, such as prolonged diarrhea, dysphagia and anal discharge. Nissapatorn *et al* (2005a,b, 2006a,b) reported similar findings.

Eighty-nine percent of patients had positive sputum for AFB and 69% had some abnormality on their chest radiographs. Ismail (2004) reported sputum is often negative for AFB, but bronchoscopy with washings for *Mycobacterial* culture gives a higher yield. In highly probable cases, empirical therapy with anti-TB drugs may be considered because it is safe and beneficial.

The diagnosis of TB is often delayed due to atypical clinical features and difficulty in obtaining positive AFB stains (Ismail, 2004), along with the fact that malignancies and other infections may present with similar symptoms as TB. Systemic symptoms, such as prolonged fever

with anorexia, weight loss and hemoptysis in an elderly patient can easily be mistaken for lung cancer. Delayed diagnosis of TB can lead to an increased period of infectivity in the community, a delay in treatment and a more severe form of the disease (Chang and Esterman, 2007).

The majority of patients in our study (65%) did not develop any complications. For those who developed complications, the most common were pleural effusion, pneumothorax and lung fibrosis. The greatest number of patients who developed complications were in the 21-40 year old age group, followed by the 41-60 year old age group. A greater impact was observed in the young and active group than in the middle age group.

The majority of patients (85%) had no complaints of side effects due to the anti-TB treatment. Among those who reported side effects, the most common problems were nausea and vomiting (41%), drug induced hepatitis (37%), blurring of vision (11%) and skin rashes and pruritis (11%). Hepatitis is a well-known side effect of anti-TB medications. Anti-TB drugs cause derangement of hepatic function revealed by clinical examination and abnormal liver function tests. The potential hepatotoxicity of some of the first-line anti-TB agents remains a problem, especially during the initial period of treatment (Shakya *et al*, 2004).

A case-control study was carried out by Pande *et al* (1996), to assess the role of age, sex, disease extent, nutritional status, past history of liver disease, infection with hepatitis viruses, acetylator status and high alcohol intake as risk factors in the development of hepatotoxicity in patients with pulmonary tuberculosis receiving anti-tuberculosis treatment. Among the various risk factors analyzed, only ad-

vanced age, hypoalbuminemia, high alcohol intake, slow acetylator phenotype, and extensive disease were risk factors for the development of hepatotoxicity.

The majority of patients in our study suffered from diabetes mellitus, hypertension, ischemic heart disease or all three conditions. Seventeen percent of patients had SLE, a renal transplant, congenital heart disease or chronic obstructive airway disease; 1% suffered from cancer. Two deaths were reported.

In two of the cases with chronic illnesses, one was a SLE patient and the other was a renal transplant patient. These 2 patients took steroids for their treatment. Prolonged treatment with immunosuppressants, such as steroids or cytotoxic drugs may predispose one to TB infection. However it cannot be deduced whether chronic diseases, such as diabetes mellitus or hypertension are directly related to susceptibility to TB infection among patients. A study by Nissapatorn *et al* (2005c) showed the risk for TB appears to increase steadily with age in diabetic patients compared to non-diabetics. They also found no differences between those with and without diabetes in regard to radiological findings. Ismail (2004) reported diabetes mellitus was a risk factor for TB.

Out of the 131 patients in our study, 16% ($n=21$) were reactivated cases (who had a history of TB at some point in their life), while 84% ($n=110$) presented with TB for the first time. Among the 28 patients who were non-compliant with their treatment, 12 were reactivated tuberculosis cases. Compliance with directly observed treatment- short course strategy (DOTS) may be affected by travel expenses, time spent traveling to a treatment center or having family members who have had the disease (O'Boyle *et al*, 2002). Defaulting on

treatment, under treatment, failure of treatment or having an immunocompromised state can lead to reactivation of TB. Defaulting on treatment can cause the bacilli to be resistant to drugs and causes further difficulty in treatment in the future. Anti-TB treatment should be accessible to patients at the nearest health center. Interventions with health education programs emphasizing the benefits of treatment compliance should be implemented in a further large-scale multi-center study (Naing *et al*, 2001).

Regarding the risk factors for TB, only 2 out of 131 patients were HIV positive and another 2 were intravenous drug users. Only 16% had contact with TB patients at some points in their lives. Venugopalan (2004), Mohamad and Naing (2004) and Nissapatorn (2003, 2006a,b) have reported TB among intravenous drug abusers and HIV patients.

In conclusion, TB has made a comeback. It has become a resurgent public health problem in developing countries in the tropics and is the leading cause of death from any single infectious agent. Non-compliance to anti-TB treatment is the most serious problem in TB control. Steps should be taken to address this resurgence immediately by improving our health care facilities, diagnostic tools and the knowledge of our health care workers. Suspected cases should be treated empirically. We should increase the awareness and knowledge of the public regarding TB and ways to stop the transmission. This can be done via mass media and health campaigns in schools, learning institutions and primary health care centers. Vaccination programs should be extensive and able to reach those who live in rural areas with limited access to health care. It should also be extended to immigrants and their children. Immigrants who enter

Malaysia should be screened thoroughly and employers who wish to employ these workers should be responsible for having them screened. Immigrant workers should also be provided with clean accommodations and good basic sanitation. Slums, low cost housing areas and rural areas should be provided with clean water, electricity and proper waste management.

ACKNOWLEDGEMENTS

The authors would like to thank the head of the Department of Medicine (Prof Wan Azman), the wonderful staff of medical records, and UMMC for their generous help and guidance in obtaining the patients' medical records.

REFERENCES

- Chang CT, Esterman A. Diagnostic delay among pulmonary tuberculosis patients in Sarawak, Malaysia: a cross sectional study. *Rural Remote Health* 2007; 7: 667.
- Dony JF, Ahmad J, Yap KT. Epidemiology of tuberculosis and leprosy, Sabah, Malaysia. *Tuberculosis* (Edinb) 2004; 84: 8-18.
- Hayati IN, Ismail Y, Zurkurnain Y. Extra-pulmonary tuberculosis: a two-year review of cases at the General Hospital Kota Bharu. *Med J Malaysia* 1993; 48: 416-20.
- Ismail Y. Pulmonary tuberculosis-a review of clinical features and diagnosis in 232 cases. *Med J Malaysia* 2004; 59: 56-64.
- Iyawoo K. Tuberculosis in Malaysia: problems and prospect of treatment and control. *Tuberculosis* (Edinb) 2004; 84: 4-7.
- Mohammad Z, Naing NN. Characteristics of HIV-infected tuberculosis patients in Kota Bharu Hospital, Kelantan from 1998 to 2001. *Southeast Asian J Trop Med Public Health* 2004; 35: 140-3.
- Mohammad Z, Naing NN, Salleh R, Ahmad N, Hamzah WM, Mahmud R. A preliminary

- study of the influence of HIV infection in the transmission of tuberculosis. *Southeast Asian J Trop Med Public Health* 2002; 33: 92-8.
- Naing NN, D'Este C, Isa AR, Salleh R, Bakar N, Mahmud MR. Factors contributing to poor compliance with anti-TB treatment among tuberculosis patients. *Southeast Asian J Trop Med Public Health* 2001; 32: 369-82.
- Nissapatorn V, Kuppusamy I, Jamaiah I, Fong MY, Rohela M, Anuar AK. Tuberculosis in diabetic patients: a clinical perspective. *Southeast Asian J Trop Med Public Health* 2005c; 36 (suppl 4): 213-20.
- Nissapatorn V, Kuppusamy I, Josephine FP, Jamaiah I, Rohela M, Khairul Anuar A. Tuberculosis: a resurgent disease in immunosuppressed patients. *Southeast Asian J Trop Med Public Health* 2006a; 37 (suppl 3): 153-60.
- Nissapatorn V, Kuppusamy I, Sim BL, *et al.* Pulmonary tuberculosis in a hospital setting: gender differences. *Public Health* 2006b; 120: 441-3.
- Nissapatorn V, Kuppusamy I, Sim BL, Quek KF, Khairul Anuar A. Tuberculosis in HIV/AIDS patients: a Malaysian experience. *Southeast Asian J Trop Med Public Health* 2005a; 36: 946-53.
- Nissapatorn V, Kuppusamy I, Wan-Yusoff WS, Anuar AK. Clinical analysis of foreign-born patients with tuberculosis found in Malaysia. *Southeast Asian J Trop Med Public Health* 2005b; 36: 713-21.
- Nissapatorn V, Kuppusamy I, Rohela M, Anuar AK, Fong MY. Extrapulmonary tuberculosis in Peninsular Malaysia: retrospective study of 195 cases. *Southeast Asian J Trop Med Public Health* 2004; 35 (suppl 2): 39-45.
- Nissapatorn V, Lee C, Fatt QK, Abdullah KA. AIDS-related opportunistic infections in Hospital Kuala Lumpur. *Jpn J Infect Dis* 2003; 56: 187-92.
- O'Boyle S J, Power J J, Ibrahim M Y, Watson J P. Factors affecting patient compliance with anti-tuberculosis chemotherapy using the directly observed treatment, short-course strategy (DOTS). *Int J Tuberc Lung Dis* 2002; 6: 307-12.
- Pande JN, Singh SP, Khilnani GC, Khilnani S, Tandon RK. Risk factors for hepatotoxicity from antituberculosis drugs: a case control study. *Thorax* 1996; 51: 132-6.
- Raviglione MC, O'Brien RJ. Tuberculosis. Harrison's principles of internal medicine. Vol 1. 14th ed. McGraw-Hill. 1998; 1: 1004-9.
- Shakya R, Rao BS, Shrestha B. Incidence of hepatotoxicity due to anti-tubercular medicines and assessment of risk factors. *Ann Pharmacother* 2004; 38: 1074-9.
- Venugopalan B. An evaluation of the tuberculosis control programme of Selangor State, Malaysia for the year 2001. *Med J Malaysia* 2004; 59: 20-5.