

A Seven Year Retrospective Study on Epidemiology and Clinical Characteristics of Tuberculosis in Iran

Simindokht Bayat¹; Ali Gol-Mohamadi¹; Mohamad Reza Sarbazi¹; Azadeh Safaee^{1,*}; Ahmad Reza Farsar¹

¹Deputy of Health, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran

*Corresponding author: Azadeh Safaee, Deputy of Health, Shahid Beheshti University of Medical Sciences, Tehran, IR Iran. Tel: +98-2144143620, Fax: +98-2144143407, E-mail: azadesa-faee@yahoo.com

Received: January 17, 2013; Revised: February 28, 2013; Accepted: March 5, 2013

Background: Tuberculosis (TB) is a major worldwide public health problem. The incidence of tuberculosis has decreased in Iran in recent years. However, despite this dramatic decline, tuberculosis is still considered to be a major health problem in Iran.

Objectives: The aim of this study was to investigate the epidemiological situation and main characteristics of tuberculosis in Iran.

Patients and Methods: The present study was designed as a retrospective study. All tuberculosis patients were included in this study during a seven year period. Patients were categorized into two groups: new and retreatment. The patients' information was extracted using a tuberculosis surveillance system. Demographic (age, gender and place of birth) and clinical characteristics included type and site of the disease, treatment outcomes, human immunodeficiency virus (HIV) co-infection and anti-TB drugs resistance.

Results: A total of 6 489 tuberculosis cases were notified during the study period. Extra-pulmonary TB was diagnosed in 30% of the cases. From 4633 pulmonary patients, 3009 new cases were categorized as smear positive pulmonary tuberculosis. Outcome evaluations demonstrated that 72% of the smear positive pulmonary patients had been cured and 7.4% had completed the duration of treatment. Co-infection of HIV existed in 3% of the patients. A drug susceptibility test was performed only for high risk patients, 34% of whom were resistant to at least one drug.

Conclusions: Our findings suggest that neither a drug resistance phenomenon nor the HIV co-infection play a dominant role in the incidence of tuberculosis in Iran. Further investigation is needed to determine the cause of the relatively high incidence of tuberculosis and its risk factors in Iran and finally considering the gap between the observed success rate and World Health Organization objectives, more accurate follow-up of patients is recommended in order to achieve complete treatment.

Keywords: Tuberculosis; Epidemiology; Tuberculosis, Multidrug-Resistant

1. Background

Tuberculosis (TB) is a major public health problem, caused by *Mycobacterium tuberculosis* (1). TB typically affects the lungs (pulmonary TB), but it can involve other organs as well (extra-pulmonary TB) (2). Adults in the economically productive age groups are more commonly affected by TB (3). TB is the seventh most common disease worldwide (1). According to a World Health Organization (WHO) report, nine million new cases of TB are diagnosed annually, and each year, about one and a half million people lose their lives due to TB infections (4, 5). The burden of disease varies depending on the geographic region, it is the highest in Asia and Africa and 40% of TB cases occur in Southeast Asia (3). Despite high expectations regarding the elimination of TB, there is evidence of the increasing incidence of this disease in some parts of the world (6, 7). The escalating number of TB cases is considered to be a consequence of the AIDS pandemic, the emergence of resistance to anti-TB

drugs and increasing levels of immigration (8-10).

WHO has evaluated the incidence of TB in six regions; the Eastern Mediterranean region, with a 7.7% incidence rate of TB has the fourth place among these regions (3). Iran is also one of the countries in this region. According to a report by the Islamic Republic of Iran Disease Control and Prevention Center, the incidence of TB has declined from 142 cases per 100 000 to 14.6 cases per 100 000 in the last 46 years (11). Declines in tuberculosis have occurred as a consequence of implementing directly observed treatment short course (DOTS) in Iran, but despite this dramatic decline, TB is still considered to be a major health problem in our country.

2. Objectives

The aim of this study was to investigate the epidemiological situation and the main characteristics of TB in Tehran, the capital of Iran, during a seven year period.

Implication for health policy/practice/research/medical education:

The results of this project could be useful in planning health and resource allocation.

Copyright © 2013, Infectious Diseases and Tropical Medicine Research Center. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

3. Patients and Methods

The present study was designed as a retrospective study. All TB cases from March 2005 to March 2011 in Shahid Beheshti University coverage area were included in this study. This university covers comprises a large area of the Tehran Province, including more than 80% of Tehran's population (about 10 million people). Tehran Province includes several rural and urban areas having heterogeneous demographical characteristics as a result of many immigrants from other cities living in this area.

For a TB diagnosis, each patient with a cough lasting for longer than two weeks underwent three sputum samples. Patients with at least two positive smear tests, one positive smear test and a suspicious chest X-ray, or one positive smear test with a positive culture, were considered as smear positive pulmonary tuberculosis (SPPT). Smear negative pulmonary tuberculosis (SNPT) was defined as ≥ 3 negative sputum smears and having suspicious clinical manifestations or chest radiographies after a course of broad spectrum antibiotics. A biopsy of the involved organ and a positive pathology report were considered essential for a diagnosis of extra-pulmonary TB. Patients were categorized into two groups: new and retreatment. A new case of TB was defined as a newly registered case of TB in a patient who had no previous history of TB treatment and a retreatment case was considered as a newly registered SPPT patient who has had received anti-TB drugs for one month or more in the past (12).

Multi drug resistance (MDR) was evaluated in patients with the results of a drug susceptibility test (DST). According to instructions from the Ministry of Health of the Islamic Republic of Iran, DST is performed only for the following groups: patients with treatment failure, chronic TB, individuals with suspicious clinical symptoms of pulmonary TB who have been in close contact with MDR-TB patients, recurrent and treatment after default cases, TB patients with HIV co-infection and SPPT prisoners. The required information was extracted from a TB surveillance system, running by health care providers in health care centers. Demographic (age, gender, and place of birth) and clinical characteristics including; type and site of the disease, outcomes of treatment, HIV co-infection, and anti-TB drugs resistance, were obtained from each patient. SPSS software, Chicago, IL, The USA (version 13) was used to analyze the data. Demographic characteristics and treatment outcomes were demonstrated by descriptive statistics (frequency and mean). Differences between the groups were determined by a Chi-square test. A P value of 0.05 or less was considered statistically significant and all reported P-values were two sided.

4. Results

There were 6 489 total TB cases notified from March 2005 to March 2011, from which 3 121 cases (48.1%) were male and 3 368 (51.9%) were female. The mean age of the

patients at diagnosis was 47.5 ± 21.8 years. The majority of patients (70%) were Iranian-born, and Afghani-born cases constituted the largest proportion of foreign born TB cases (99%). More than 80% of the patients resided in urban areas. Extra-pulmonary tuberculosis was diagnosed in 30% of the cases ($n = 1\,947$), and lymphatic TB was the most common site for extra-pulmonary TB (27.6%), followed by bone TB (15.9%). The site distribution and types of TB are demonstrated in Table 1.

Extra-pulmonary TB was most prevalent in women ($P < 0.0001$). Moreover, the mean age of the extra-pulmonary TB patients was significantly younger than the pulmonary TB patients (40.3 years vs. 50.4 years, $P < 0.0001$). An HIV test was not done for all TB cases. Of the 917 TB patients with a reported HIV result, 203 patients had a co-infection with HIV. The risk of a positive HIV test in the pulmonary TB cases was slightly higher than in the extra-pulmonary TB patients (Table 2). Of the 4 633 pulmonary patients, 3 009 new cases were categorized as SPPT and 1 073 cases were considered as SNPT. Smear results in 209 patients during the initial treatment period were unspecified. Outcome evaluations demonstrated that 72% of the SPPT patients had been cured, 7.4% of whom had completed the duration of treatment (Table 3).

Table 1. Distribution of Tuberculosis According to Type and Site of the Disease

Variables	No. (%)
Pulmonary TB^a	4540 (70.0)
Smear positive	3009 (66.3)
Smear negative	1073 (23.5)
Smear unspecified	117 (2.6)
Retreatment	344 (7.6)
Extra-pulmonary TB^b	1947 (30.0)
Meningeal TB	82 (4.1)
Peritoneal TB	58 (2.9)
Pericardial TB	45 (2.2)
Miliary TB	41 (2.0)
Cutaneous TB	52 (2.6)
Gastrointestinal TB	74 (3.7)
Ocular TB	81 (4.0)
Genital TB	172 (8.5)
Bone TB	320 (15.9)
Lymphatic TB	556 (27.6)
Other	533 (26.5)

^a Abbreviation: TB, tuberculosis.

^b Some extra-pulmonary patients had more than one organ affected with TB.

Table 2. Comparison Between Characteristics of Pulmonary and Extra-Pulmonary TB Patients

	Pulmonary TB ^a , No. (%)	Extra-pulmonary TB, No. (%)	P value
Gender			< 0.0001
Male	2277 (50.2)	844 (43.3)	
Female	2263 (49.8)	1103 (56.7)	
Place of birth			0.213
Born in Iran	3169 (69.8)	1379 (70.8)	
Born abroad	1371 (30.2)	568 (29.2)	
HIV co-infection^a			< 0.001
Positive HIV	165 (24.7)	37 (14.8)	
Negative HIV	502 (75.3)	213 (85.2)	
MDR^a			< 0.0001
Resistant	37 (0.8)	2 (0.1)	
Not resistant	4503 (99.2)	1945 (99.9)	

^a Abbreviations: HIV, human immunodeficiency virus; MDR, multi drug resistant; TB, tuberculosis.

Table 3. Treatment Outcomes in Tuberculosis Patients Between 2005 and 2011

	New Cases, No. (%)				Retreatment ^b , No. (%)
	Smear Positive TB ^a	Smear Negative TB	Smear Unspecified	Extra-pulmonary TB	
Cured	2158 (71.7)	NA ^a	NA	NA	144 (41.9)
Completed	222 (7.4)	848 (79)	80 (68.5)	1416 (72.7)	62 (18)
Death	202 (6.7)	66 (6.1)	13 (11.1)	70 (3.6)	21 (6)
Failure	47 (1.6)	3 (0.3)	0 (0)	4 (0.2)	13 (3.8)
Defaulted	135 (4.5)	42 (4)	4 (3.4)	56 (2.9)	32 (9.4)
Transferred out	40 (1.3)	9 (0.8)	0 (0)	25 (1.5)	4 (1.3)
Transferred in	64 (2.1)	21 (2)	1 (0.8)	38 (1.9)	11 (3.3)
Not assessed	120 (4)	37 (3.4)	14 (11.9)	59 (3.1)	51 (14.8)
Misdiagnosed	21 (0.7)	47 (4.4)	5 (4.3)	275 (14.1)	5 (1.5)

^a Abbreviations: NA, not available; TB, tuberculosis.

^b Retreatment including recurrent, treatment failure, treatment after default and multi drug resistant cases.

In total, 369 deaths occurred during the study period, with 71 cases (19%) directly related to the TB infection, while the other causes of deaths were unclear or due to competition risk. There were 124 patients (1.9%) who reported at least one major side effect of therapy, and jaundice (1.4%) was reported as the most common side effect of the therapy. A drug susceptibility test (DST) was performed for only 114 patients, 34% of whom were resistant to at least one drug.

5. Discussion

In this retrospective study, we evaluated the epidemiological and clinical characteristics of TB cases using a TB surveillance data system over a seven year period. In total, 6489 patients were reviewed, and about two-thirds of

them had contracted pulmonary TB. Our findings showed a slightly higher proportion of female TB patients, which could be due to the greater level of attention women give to their health status, health seeking behavior differences or the social and economical inequalities between men and women. (13-15). In contrast with other studies (5, 16, 17), the distribution of TB in immigrant patients was lower than in the Iranian-born patients. As previously mentioned, many immigrants from other cities of Iran live in our study area, and these individuals commonly suffer from problems such as; poverty, addiction and malnutrition. This may be the reason for the higher number of Iranian-born TB patients in the study than foreign-born patients. As noted in the results, only 14% of the high risk TB patients were tested for HIV co-infection and the test was positive for 22%

of them. These results are not entirely satisfactory and we may lose some TB-HIV patients, however, taking into consideration that Iran is in a low rate area of co-infection, the screening of high risk patients for HIV co-infection could be more effective than screening all patients (10).

The success rate of treatment in this study was reported to be 79%, which is lower than the WHO target, which could be due to the poor follow-up in the early years of this study. Of course the follow-up of patients has improved significantly in recent years, but the success rate is calculated for the entire seven year period, so the calculated rate has declined, influenced by deficits from the early years of the study. Treatment failure rates were reported to be less than 2%, which is consistent with the objectives of WHO, which could also be an indicator of the low-level drug resistance in Iran. Consequently it seems that performing DST in the high risk group is sufficient and it is not essential does to test all patients. Similar studies conducted in Nepal (13) and Turkey (18) showed that the lymph nodes were the most common site of extra-pulmonary TB, although the localization of extra-pulmonary TB may be variable in different studies. Our study found a strong association between younger age and female sex with extra-pulmonary TB, which may be due to the type of activity and exposure of these individuals with special risk factors.

Moreover, in this present study, extra-pulmonary TB was negatively related to MDR and HIV co-infections. Although HIV infection has been considered as a contributing factor to the increasing numbers of extra-pulmonary TB, we found a negative association between extra-pulmonary and HIV co-infection. This may be attributable to the different definition of extra-pulmonary TB in various studies (10, 19). Hence, in most studies (10, 19, 20) the evaluation of the association of HIV co-infection and extra-pulmonary TB was conducted according to the site of the disease, in contrast with the present study. It is also of importance to note that disseminated TB was categorized as extra-pulmonary TB in this study.

This study had some limitations. Sociodemographical data such as life style factors and economic status were not available. In addition, the HIV status in most of the patients was missing or unknown. In summary, according to our observation, neither a drug resistance phenomenon nor the HIV co-infection plays a dominant role in TB incidence in Iran. Further investigation is needed to determine the cause of the relatively high incidence of TB and its risk factors in Iran. Although extra-pulmonary TB case finding is not a priority in TB control programs, giving more attention to symptoms of this type of TB in women and younger people could lead to earlier diagnosis and a decrease in TB mortalities. In conclusion, considering the gap between the observed success rate and the objectives of World Health Organization, more accurate follow-up of patients is recommended in order to achieve complete treatment.

Acknowledgements

We would like to thank the health care providers and physicians of the health service centers in Shahid Beheshti University of Medical Sciences for their valuable collaboration in this study.

Authors' Contribution

Study concept and design: Dr. Simindokht Bayat; acquisition of data: Dr. Ahmad Reza Farsar; analysis and interpretation of data: Azadeh Safaee and Dr. Ali Golmohamadi; drafting of the manuscript: Azadeh Safaee; critical revision of the manuscript for important intellectual content: Dr. Mohamad Reza Sarbazi; statistical analysis: Azadeh Safaee; administrative, technical and material support: Dr. Ali Golmohamadi; study supervision: Dr. Ali Golmohamadi and Dr. Ahmad Reza Farsar.

Financial Disclosure

We have no financial interests related to the material in the manuscript.

Funding/Support

The study did not receive any financial support.

References

1. Wangdi K, Gurung MR. The epidemiology of tuberculosis in Phuentsholing General Hospital: a six-year retrospective study. *BMC Res Notes*. 2012;**5**:311.
2. Saif Alfaresi M, Hag-Ali M. Susceptibility Pattern and Epidemiology of Mycobacterium tuberculosis in United Emirati Hospital. *Open Microbiol J*. 2010;**4**:1-4.
3. *Global tuberculosis report*. Geneva:WHO;2012. Available from: http://apps.who.int/iris/bitstream/10665/75938/1/9789241564502_eng.pdf.
4. Fortun J, Martin-Davila P, Navas E, Lopez-Velez R, Pintado V, Cobo J, et al. Changes in the epidemiology of tuberculosis: the influence of international migration flows. *Enferm Infecc Microbiol Clin*. 2011;**29**(9):654-9.
5. Odone A, Ricco M, Morandi M, Borrini BM, Pasquarella C, Signorelli C. Epidemiology of tuberculosis in a low-incidence Italian region with high immigration rates: differences between not Italy-born and Italy-born TB cases. *BMC Public Health*. 2011;**11**:376.
6. Khazaei HA, Rezaei N, Bagheri GR, Dankoub MA, Shahryari K, Tahai A, et al. Epidemiology of tuberculosis in the Southeastern Iran. *Eur J Epidemiol*. 2005;**20**(10):879-83.
7. Cruz-Ferro E, Fernandez-Nogueira E. Epidemiology of tuberculosis in Galicia, Spain, 1996-2005. *Int J Tuberc Lung Dis*. 2007;**11**(10):1073-9.
8. Merza MA, Farnia P, Tabarsi P, Khazampour M, Masjedi MR, Velayati AA. Anti-tuberculosis drug resistance and associated risk factors in a tertiary level TB center in Iran: a retrospective analysis. *J Infect Dev Ctries*. 2011;**5**(7):511-9.
9. Diz S, Lopez-Velez R, Moreno A, Fortun J, Moreno L, Gomez-Mampaso E, et al. Epidemiology and clinical features of tuberculosis in immigrants at an infectious diseases department in Madrid. *Int J Tuberc Lung Dis*. 2007;**11**(7):769-74.
10. Garcia-Rodriguez JF, Alvarez-Diaz H, Lorenzo-Garcia MV, Marino-Callejo A, Fernandez-Rial A, Sesma-Sanchez P. Extrapulmonary tuberculosis: epidemiology and risk factors. *Enferm Infecc Microbiol Clin*. 2011;**29**(7):502-9.
11. Ministry of Health and Medical Education of Islamic Republic of

- Iran. [Incidence of Tuberculosis in Iran]. Available from: http://cdc.hbi.ir/TB_Situation.aspx/2011.
12. Shao Y, Yang D, Xu W, Lu W, Song H, Dai Y, et al. Epidemiology of anti-tuberculosis drug resistance in a Chinese population: current situation and challenges ahead. *BMC Public Health*. 2011;**11**:110.
 13. Sreeramareddy CT, Panduru KV, Verma SC, Joshi HS, Bates MN. Comparison of pulmonary and extrapulmonary tuberculosis in Nepal- a hospital-based retrospective study. *BMC Infect Dis*. 2008;**8**:8.
 14. Hudelson P. Gender differentials in tuberculosis: The role of socio-economic and cultural factors. *Tubercle Lung Dis*. 1996;**77**(5):391-400.
 15. Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. *Int J Tuberc Lung Dis*. 1998;**2**(2):96-104.
 16. Menzies HJ, Winston CA, Holtz TH, Cain KP, Mac Kenzie WR. Epidemiology of tuberculosis among US- and foreign-born children and adolescents in the United States, 1994-2007. *Am J Public Health*. 2010;**100**(9):1724-9.
 17. Andersen RM, Bjorn-Praest SO, Gradel KO, Nielsen C, Nielsen HI. Epidemiology, diagnostic delay and outcome of tuberculosis in North Jutland, Denmark. *Dan Med Bull*. 2011;**58**(3):eA4256.
 18. Musellim B, Erturan S, Sonmez Duman E, Ongen G. Comparison of extra-pulmonary and pulmonary tuberculosis cases: factors influencing the site of reactivation. *Int J Tuberc Lung Dis*. 2005;**9**(11):1220-3.
 19. 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**(9):1350-7.
 20. Kingkaew N, Sangtong B, Amnuaiphon W, Jongpaibulpatana J, Mankatittham W, Akksilp S, et al. HIV-associated extrapulmonary tuberculosis in Thailand: epidemiology and risk factors for death. *Int J Infect Dis*. 2009;**13**(6):722-9.