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Osteoarticular Tuberculosis in Iran, 2002 to 2011

Mohammad Javad Nasiri¹, Mohammad Varahram^{1*}, Mahdi Shams¹,
Kimia Taghavi¹, Parissa Farnia¹ and Ali Akbar Velayati¹

¹*Mycobacteriology Research Centre, National Research Institute of Tuberculosis and Lung Disease [NRITLD], Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.*

Authors' contributions

This work was carried out in collaboration between all authors. Authors PF and AAV designed the study and wrote the protocol. Author MJN wrote the manuscript and managed the literature analyses. Authors MV, MS and KT participated in data analysis. All authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Introduction: Tuberculosis (TB) still causes serious illnesses in millions of people throughout the world. Although pulmonary TB accounts for the majority of the cases, extrapulmonary TB (EPTB) also contributes to the burden of disease and frequently neglected in the national TB control programs. The present study was designed to investigate the frequency of osteoarticular TB (OT), one of the most common sites of EPTB, in Iran.

Material and Methods: Clinical and laboratory data of patients diagnosed with TB was retrospectively analyzed (September 2002 and December 2011). Identification of *Mycobacterium tuberculosis* was performed using conventional and molecular methods. The associated risk factors were evaluated using the Chi-square test.

Results: Out of 725 patients with culture-proven EPTB, 10 (1.3%) were OT cases. According to the statistical analysis, patient characteristics (gender, age, nationality) were not significantly associated with OT ($p > 0.05$).

Conclusions: Our finding showed that the prevalence of OT in our study was relatively low over the last decade. However, further studies would be necessary to elucidate the exact magnitude of OT in Iran.

*Corresponding author: E-mail: MVarahram@nritld.ac.ir;

Keywords: Tuberculosis; osteoarticular; Iran.

1. INTRODUCTION

Tuberculosis (TB) still causes serious illnesses in millions of people throughout the world and is one of the leading causes of death from an infectious disease. According to the latest report released by World Health Organization (WHO), there were an estimated of 8.6 million incident cases of TB in 2012 and 1.3 million deaths [1]. Out of all TB cases, approximately 12% were considered to have extrapulmonary TB (EPTB) [1]. Infection in bones and joints, also known as osteoarticular TB (OT), are among the most common sites of EPTB [2]. Clinical manifestations of OT are frequently nonspecific and patients may be easily misdiagnosed as brucellosis, rheumatoid arthritis or aspergillus spondylitis [2-4]. Thus, this deferment in diagnosis of OT cases can leads to severe complications such as joint destruction and even paralysis. In Iran, of 10,705 new cases of TB that were notified in the year 2012, 3,105 had EPTB [5]. However, the exact magnitude of various forms of EPTB is rarely addressed in the public health literature. There is a need to investigate the frequency of OT patients among all TB cases.

2. MATERIALS AND METHODS

2.1 Setting and Study Population

This retrospective study was performed at the Mycobacteriology Research Centre (MRC). MRC is the only national reference TB laboratory of Iran which is supervised by Swedish Institute for Infectious Disease Control. The study included the review of personal characteristics (age, gender, nationality, place of residency) of TB cases who submitted clinical samples (for microscopy examination and culture) to the center between September 2002 and December 2011. A case of OT was defined as a patient with one or more osteoarticular samples (bone biopsy, synovial biopsy or synovial fluid) positive for *Mycobacterium tuberculosis* by culture. The most common symptoms of patients with OT were stiffness, painful restricted joint movements and severe spasm of the surrounding muscles. The study was approved by the ethics committee of MRC.

2.2 Clinical Samples

Specimens submitted for bacteriological confirmation included bone biopsy, synovial biopsy and synovial fluid taken from the site of the infection. Samples were collected in sterile containers from each patient and were used to do microscopy and culture for mycobacteria. All specimens were held at 4°C until processed by standard laboratory procedures [6]. The majority of specimens were processed within 24 h at the TB laboratory.

2.3 Isolation of Mycobacterium Tuberculosis

Samples from each patient were decontaminated by Petroff's method and were inoculated into Lowenstein-Jensen media [7]. Bacterial isolates identified as *M. tuberculosis* complex using molecular methods, including spoligotyping analysis as described elsewhere [8].

2.4 Statistical Analysis

Statistical analysis was carried out using SPSS version 18 (SPSS Inc., Chicago, IL, USA). Associations of variable (age group, gender, nationality) with the OT were assessed using the Chi-square test. p values less than 0.05 were considered statistically significant.

3. RESULTS

During 2002-2011, the number of cases diagnosed with TB was 4,950, of which 725 (14.6%) were EPTB and the remaining 4225 (85.4%) were Pulmonary TB (PTB) (Table 1). Of 725 EPTB, 10 (1.3%) were from OT cases, while 715 were from other EPTB including pleural TB, lymphatic TB, skin TB, and genitourinary TB. Characteristics of the 966 study cases (956 PTB cases and 10 OT cases) whose records were available are shown in Table 2. Statistical analysis of patient characterization indicated that gender, age and nationality are not significantly associated with OT (Table 2). To analyses the trend and the burden of OT in Iran, results from our study were compared with those of previous studies (Table 3).

Table 1. Prevalence of EPTB in Iran during 2002 to 2011

Study period	Total no. of TB cases (%)	No. of PTB* (%)	No. of EPTB* (%)
2002-2011	4950 (100)	4225 (85.4)	725** (14.6)

*PTB, Pulmonary TB; EPTB, Extrapulmonary TB.

**Of 725 EPTB, 10 (1.3%) were osteoarticular TB.

Table 2. Association of patient characteristics with OT

	PTB cases [956]	Osteoarticular TB [10]	P-value	OR (CI 95%)
Gender				
Female	329 [34.4]	2 [20.0]	0.3	0.4 (0.1-2.2)
Male	627 [65.6]	8 [80.0]		
Age				
<45	461 [48.2]	7 [70.0]	0.1	2.5 (0.6-9.7)
>45	495 [51.8]	3 [30.0]		
Nationality				
Iranian	778 [81.4]	9 [90.0]	0.4	0.4 (0.06-3.8)
Afghans	178 [18.6]	1 [10.0]		

Table 3. Prevalence of osteoarticular TB in different regions of Iran

Region of study	No. of study	Year of studies	n/N*	Prevalence of OT (95% CI)	Reference
Central parts of Iran	4	1996-2008	122/621	19.6 (16.7-22.9)	[10,19-21]
East of Iran	3	1994-2006	79/731	10.8 (8.7-13.2)	[22-24]
North of Iran	2	1990-2005	26/287	9.0 (6.0-12.0)	[9,25]
West of Iran	1	2004-2010	9/134	6.7 (3.5-12.2)	[26]
Current study	-	2002-2011	10/725	1.3 (0.7-2.5)	-

*n, number of OT cases; N, total number of EPTB

4. DISCUSSION

Understanding the magnitude of EPTB is one of the major priorities in improvement of national TB control programs. However, the prevalence of this kind of disease, especially those with osteoarticular involvement, is rarely addressed in the public health literature. In this regard, clinical and laboratory data of patients diagnosed with TB was retrospectively analyzed to evaluate the prevalence of OT.

According to our study, the overall rate of OT was 1.3% over the study period. The documented osteoarticular cases in our results were lower than those of previous studies from Iran with overall cases ranges from 4.8-21.0% [9-10]. As shown in Table 3, the prevalence of OT in the surveys that conducted in the central regions of the country was relatively high as compared with other area. Most of the healthcare laboratories in the central parts of Iran have proper facilities to admit TB patients. Thus, the high incidence of OT in these areas may be attributed to referring of patients from other provinces to these regions for further investigations. Our study also revealed low rates of OT compared with studies reported by neighboring countries i.e. Turkey and Afghanistan [11,12]. The low rate of OT might be due to the fact that most of the patients attending to the referral centre were PTB cases.

Although the prevalence of OT was relatively low in our study, special attention should be paid to these groups of patients. The importance of OT could be discussed in various ways. First of all, the national TB control programs in Iran, designed mainly for pulmonary forms of disease, recommend the use of standardized short-course chemotherapy to all confirmed sputum smear-positive cases, a system of regular drug supply and a monitoring system for programs supervision. These guidelines do not provide specific recommendations for OT. Secondly, clinical manifestations of OT are frequently nonspecific and most patients easily could be misdiagnosed as brucellosis, a disease that is endemic in Iran. Consequently, these cases may receive specific drugs (i.e. widespread use of streptomycin, the most effective drug against brucellosis), which can results in increased risk of acquiring new drug resistance i.e. drug resistant TB [13,14].

Our results showed no association between patient characteristics and OT cases. As shown in Table 2, most of the osteoarticular cases were among the young age group. However no statistical association was observed among the osteoarticular distribution in different age groups. The association of age and OT was controversial in different studies [15]. An analysis in Spain and Nigeria identified younger age as important risk factors for osteoarticular cases [16,17]. However, other authors mention that patients more than 45 years are said to constitute the group at the higher risk for OT [18].

Some limitations of this study should be considered for results interpretation. First, the result cannot entirely represent the prevalence of OT in Iran because it doesn't serve the total population of the country. Second, the clinical description of cases; the median length, main joints involved, and main symptoms could not be considered due to the limited information obtained from the included patients.

5. CONCLUSION

Our results showed that the prevalence of OT in our study was relatively low over the last decade. However, further studies would be necessary to elucidate the exact magnitude of OT in Iran.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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