A NOVEL STUDY OF VALIDITY OF LATENT TUBERCULOSIS AS A PREDICTOR TO TUBERCULOSIS OF THORACIC SPINE

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ABSTRACT

Objective: The objective of this study is to assess the validity of latent tuberculosis (TB) as a predictor for TB of thoracic spine.

Methods: This cross-sectional study involved 31 patients with osteoarticular TB diagnosed on the base of clinical features, magnetic resonance imaging, and tissue biopsy. Patients' demographic and clinical characteristics of the disease were recorded. Latent TB was diagnosed by tuberculin skin test (TST) >10 mm.

Results: The mean age of patients was 44.9 ± 19.0 years. Females were 17 (54.8) and mean body mass index was 24.6 ± 4.9 kg/m^2. Thoracic spine was the highest osteoarticular TB site. Then, lumbar spine TB was 3 (9.7%) patients. Third in rank was TB of the knee joints 2 (6.5%). Cervical spine and hip joint TB were each one, 1 (3.2) patients, respectively. Validity of latent TB as a test to predict TB of thoracic spine revealed that if TST was positive, then this test will be accurate in 77.42% and we can establish the diagnosis of TB of the thoracic spine with 90.48% confidence if we had a clinical suspicion of TB of thoracic spine.

Conclusion: There was a significant positive correlation between osteoarticular TB and latent TB. Thoracic spine TB was the most common osteoarticular TB infection compared to other sites. Patients who had latent TB have 9.5 times risk of having TB of the thoracic spine. Latent TB was a valid measure to predict TB of thoracic spine.

Keywords: Latent tuberculosis, Osteoarticular tuberculosis, Tuberculosis

INTRODUCTION

Tuberculosis (TB) is a multisystemic chronic infection caused by *Mycobacterium* TB and considered a major global health issue worldwide with 8.8 million people developing TB annually [1,2]. Drug-resistant TB developed due to improper treatment or interruption of treatment [3], and according to the latest WHO estimate, it ranks as the second leading cause of death from an infectious disease worldwide after the human immunodeficiency virus. Most of the estimated number of cases in 2011 were reported in Asia (59%) and Africa (26%) [4]. Osteoarticular TB is an uncommon form of extrapulmonary TB (EPTB) and comprises 1–6% of all TB cases and 10–15% of all EPTB cases [5,6]. Osteoarticular TB can cause significant morbidity, and a high index of suspicion is needed for early diagnosis so as to avoid destruction and disability [7]. Even with adequate medical and surgical treatment, osteoarticular TB can be associated with morbidity and mortality [8]. EPTB usually takes the form of arthritis or osteomyelitis. Rarely. it can present as tenosynovitis or bursitis. The common sites of involvement are spine and weight-bearing joints. Studies available on extrapulmonary TB, with reference to incidence and bacteria positivity, are scarce [9]. Musculoskeletal TB has been infrequently reported, especially in the developed world [10].

Latent TB infection (LTBI) is characterized by the presence of immune responses to *Mycobacterium* TB infection without clinical evidence of active TB [11,12]. A vast majority of infected persons have no signs or symptoms of TB disease and are not infectious, but they are at risk for developing active TB disease and becoming infectious [13]. The tuberculin skin test (TST) is widely used and inexpensive test to diagnose latent TB, but it has poor specificity and sensitivity [14]. Up to knowledge, there was no previous study on correlation between osteoarticular TB and latent TB. This study was designed to assess the correlation between osteoarticular TB and latent TB.

PATIENTS AND METHODS

Study design

This cross-sectional study was conducted in outpatient clinics in Baghdad Teaching Hospital and National TB specialized center, Baghdad, Iraq, from June 2016 to December 2016. Ethical approval was taken from the Department of Medicine, College of Medicine, University of Baghdad, and an informed written consent was obtained from each patient participated in the study.

Sample selection

Patients included in the study were those with any age and sex with TB osteoarticular diagnosed according to clinical and laboratory investigation and proved with tissue biopsy that was referred to the outpatient clinics in National TB specialized center.

Data entry, collection, and evaluation

Data were collected using questionnaire and interview with the patients who were seen consecutively. Sociodemographic and clinical data were collected and included age, sex, body mass index, history of contact with TB, history of pulmonary TB, smoking history, history of comorbid diseases like diabetes, renal impairments, and history of immune suppressants intake.

Outcome measurements

Latent TB was diagnosed by TST in millimeters [15], and TB site location was determined by magnetic resonance imaging (MRI).

TST was done by an intradermal injection of 2TU of Statens Serum Institut (SSI) tuberculin RT23 in 0.1 ml solution for injection. The reaction will be read 48 to 72 hours later and we measure the diameter of induration across the forearm in millimeters. If there is no induration,

the result should be recorded as "0 mm" A test >10 mm was considered positive for our patients [16,17].

Statistical analysis

Anderson darling test was done to asses if continuous variables follow a normal distribution. All variables follow normal distribution which were expressed as mean±standard deviation. Categorical variables were presented using numbers and percentage. Difference between categorical variables was measured using Fisher's exact test. Binary logistic regression analysis was used to assess the relationship between latent TB and TB site. SPSS 20.0.0 and Minitab 17.1.0 were used to perform the statistical analysis, p<0.05 was considered statistically significant.

RESULTS

Mean age of the patients was 44.9 ± 19.0 years ranging from 10 to 70 years, while mean BMI 24.6 ± 4.9 kg/m^2 ranging from 15.53 to 34.37, and females were 54.8%. Other clinical characteristics are shown in Table 1.

The highest prevalence of osteoarticular TB was thoracic spine TB 24 patients (77.4%) as shown in Fig. 1.

Fig. 2 shows that prevalence of patients with thoracic spine TB who had latent TB was significantly higher than other TB of other locations (19 [79.2%] vs. 2 [28.6%], p=0.022).

Patients with latent TB (TST>10 mm) had significantly higher risk of having thoracic TB compared to those patients who did not have latent TB. Latent TB increases the risk of having thoracic spine TB by 9.5 times as shown in Table 2.

Validity of latent TB as a test to predict TB of thoracic spine revealed that if TST was positive, then this test will be accurate in 77.42% and we can establish the diagnosis of TB of thoracic spine with 90.48% confidence if we had clinical suspicion of TB of thoracic spine as shown in Table 3

DISCUSSION

This cross-sectional study showed a significant positive correlation between osteoarticular TB and latent TB. Thoracic spine TB was the most common osteoarticular TB infection compared to other sites. Patients who had latent TB had 9.5 times risk of having TB of thoracic spine. This finding is clinically important and suggests that patients with latent TB have a high risk of osteoarticular TB infection, especially TB spine. Therefore, patients with latent TB will give us high index of suspicion of the early diagnosis and appropriate treatment of TB spine to prevent its neurological complications or spinal deformity instability.

This osteoarticular TB may be caused by reactivation of bacilli lodged in bone during the original mycobacteria of primary infection. The predilection of the bacillus for the spine and large joints may be related to the heavy vascular supply of the vertebra and growth plates of the long bones. Furthermore, it is believed to result from extension of a primary infectious focus in the bone to the joint. And it is Infrequently to be just: Tuberculous bacilli travel from the lung to the spine along the Batson paravertebral venous plexus or by lymphatic drainage to the paraaortic lymph nodes [17].

Similar to the current study, Pigrau-Serrallach and Rodríguez-Pardo reported that tuberculous vertebral osteomyelitis affects the thoracic or thoracolumbar segment in around half of the cases, followed by the lumbar segment, and to a much lesser extent, the cervical segment [18].

Some studies observed that TB spine was the most common site of articular TB. TB spine was reported to be 64% in Mateo *et al.* study [19] and 49% in Houshian *et al.* study [20]. Other studies showed that multifocal non-contiguous spinal involvement is reported to be

Table 1: Demographic and clinical features of the patients

Variables	Values
Age (years), mean±SD (range)	44.9±19.0 (10–70)
BMI (kg/m^2)	24.6±4.9 (15.53–34.37)
Gender n(%)	
Male	14 (45.2)
Female	17 (54.8)
History of TB contact n(%)	2 (6.5)
History of pulmonary TB infection n(%)	2 (6.5)
Immunosuppressant use n(%)	3 (9.7)
Diabetes history n(%)	5 (16.1)
Ischemic heart disease history n(%)	2 (6.5)
Hypertension n(%)	5 (16.1)
Renal impairment n(%)	1 (3.2)
Smokers n(%)	18 (58.1)

BMI: Body mass index, TB: Tuberculosis, SD: Standard deviation, n: Number, %: Percent

Table 2: Logistic regression analysis to assess the correlation between thoracic spine TB and latent TB

Variable	OR 95% CI	p value
TST positive	9.5 1.403–64.346	0.021

Binary logistic regression, OR: Odd ratio, 95% CI: 95% Confidence interval, TB: Tuberculosis

Table 3: Validity of latent TB as a predictor to TB of thoracic spine

Parameter	Sensitivity	Specificity	Accuracy	PPV	NPV
Latent TB positive (%)	79.17	71.43	77.42	90.48	50

PPV: Positive predictive value, NPV: Negative predictive value, TB: Tuberculosis
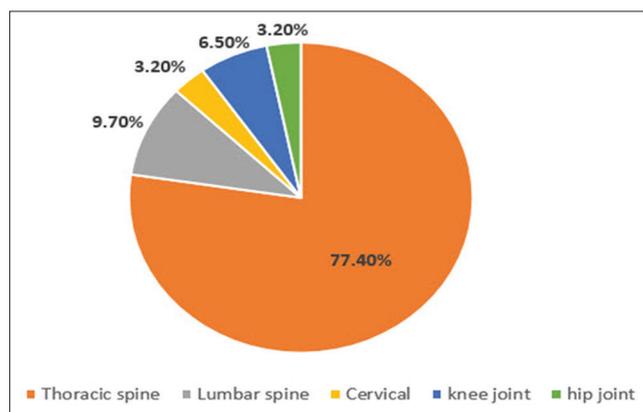
Fig. 1: Osteoarticular distribution of tuberculosis

uncommon and observed in 16.3–71.4% of cases when whole-body MRI is performed [21-23]. It was more common in areas that have a high prevalence of mycobacterial infection, such as South Africa [23]. However, the risk of having TB of the thoracic spine if they had latent TB and its validity as a predictor for TB of thoracic spine was not reported in the previous studies.

The main limitation of the present study was a small sample of patients and may be solved by a larger prospective study; however, it is the first study that reports a correlation between osteoarticular TB and latent TB.

In conclusion, osteoarticular TB significantly associated with latent TB and those patients with latent TB had a high risk of having thoracic spine TB, and latent TB is a valid measure for predicting TB of thoracic spine.
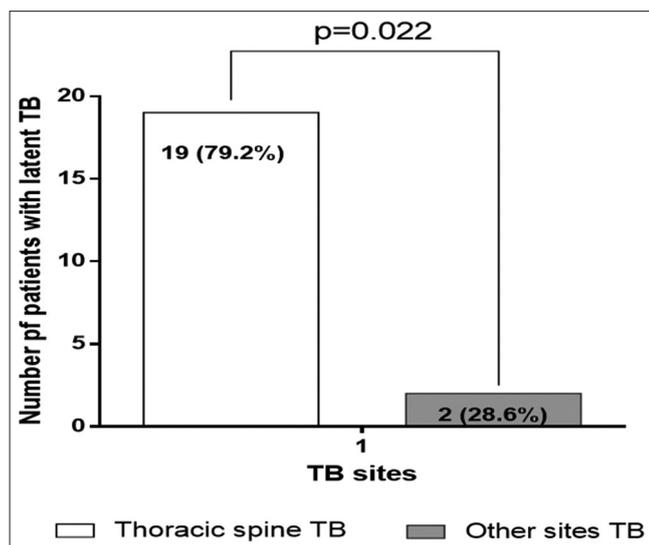
Fig. 2: Comparison between thoracic spine tuberculosis (TB) and other sites according to the presence of latent TB

This suggests that screening for latent TB may help in prediction of osteoarticular TB and early diagnosis and subsequently better treatment response with prevention of spinal and neurological complications.

AUTHOR'S CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Gorial had full access to all of the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design: Faiq I. Gorial, Mohammad Yahya Abdulrazaq, and Hayder Adnan Fawzi.

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Analysis and interpretation of data: Faiq I. Gorial, Mohammad Yahya Abdulrazaq, and Hayder Adnan Fawzi.

CONFLICTS OF INTEREST

All the authors hereby declare that there is no conflict of interest.

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