Tuberculin Skin Test Positivity in Hospitalized Patients in Baghdad Teaching Hospital

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ABSTRACT

Background: One third of earth population are infected with *Mycobacterium tuberculosis*. In the majority, infection is asymptomatic (latent) and is detected by positive tuberculin skin test. It constitutes an important source of infection and may activate later in life. Iraq has been identified as middle-TB burden country in the world.

Objectives: To determine the frequency of latent tuberculosis infection among patients admitted to a medical ward in Baghdad teaching hospital.

Methods: One hundred and thirty three adult patients of both genders free of any evidence of active tuberculosis were included in the study. The Mantoux technique was used and two units of purified protein derivative were applied by an intradermal injection in the middle third of the inner forearm. Skin reaction was quantified 48 to 72 hours after the injection and considered positive with induration of ≥10 mm.

Results: A positive tuberculin skin test result was observed in 13 patients (9.8%). Two patients (15.4%) were ≤ 45 year old, 8 patients (61.5 %) between ages of 46-65 and 3 patients (23.1%) older than 65 years. Eight responders (61.5%) were males. Among TST positive group, six patients (46.2%) had spent some time in prison, whereas only three patients (2.5%) of TST negative group reported such story**.**

Conclusion: History of incarceration is the only factor associated with significant tuberculin reactivity among hospitalized patients in a single medical unit in Baghdad teaching hospital.

Keywords: Latent tuberculosis, Active tuberculosis, Tuberculin skin test.

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Tuberculosis remains a major global health problem. It causes ill health among millions of people each year and ranks as the second leading cause of death from an infectious disease worldwide[1]. It is caused by bacteria of the *Mycobacterium tuberculosis* complex and usually affects the lungs, although other organs are involved in up to one-third of cases[2]. In more than 90% of persons infected with *M. tuberculosis,* the pathogen is contained as asymptomatic latent infection[3].

Iraq has been identified as middle-TB burden country in the world[4]. Chest and respiratory disease institute report 2012, gives an estimated incidence of all TB cases in Iraq at 45/100,000 population, a notified rate of 8/100,000 population for new sputum smear positive pulmonary tuberculosis and an estimated prevalence of all TB cases at 73/100,000 population[5]. One of the key challenges to greater progress in TB control is the reservoir of latent TB infection (LTBI)[6].

Latent tuberculosis infection is defined by the presence of an *M. tuberculosis* specific immune response in the absence of clinical and radiological disease[7]. The risk of active disease is estimated to be approximately 5% in the 18 months after initial infection and then approximately 5% for the remaining lifetime. Several host factors, including age of less than 5 years, HIV co-infection, diabetes mellitus, smoking, undernutrition, chronic renal failure, and iatrogenic immunosuppression, increase the risk of progression to active TB in remotely infected individuals[6].

The assessment of latent infection relies on measurement of host immune responses as a surrogate for the presence of viable bacteria[8]. Latent infection can be diagnosed with either a tuberculin skin test or an interferon gamma release assays.

Tuberculin skin test (TST) involves intradermal inoculation of purified protein derivative (PPD) "tuberculin" which leads to delayed type hypersensitivity response causing cutaneous induration at the site of injection which peaks at 48-72 hours[9]. Interferon-gamma release assays (IGRAs) for TB are based on exposing T-lymphocytes ex vivo to *Mycobacterium tuberculosis*-specific antigens[10].

The aim of this study is to determine the frequency of latent tuberculosis infection among patients admitted to a medical ward in Baghdad teaching hospital by mean of TST, and to assess its correlations with sociodemographic characteristics and medical conditions of the study population.

Methods

Patients of both sexes, aged ≥ 15 year were included in the study. They were admitted to the fifth medical ward in Baghdad teaching hospital during the period from June 2013 to January 2014.

A standardized questionnaire was filled for each patient, including enquiry about sociodemographic characteristics, contact with a patient with tuberculosis, previous episodes of tuberculosis and specific therapy, smoking habit, injection drug use, use of corticosteroid or immunosuppressive therapy, chronic medical illness (e.g., diabetes mellitus, chronic kidney disease) and malignancy, history of incarceration, and family size. All patients were carefully questioned about specific symptoms (cough, hemoptysis, fever, night sweats and weight loss) and examined physically to exclude features of active tuberculosis.

The TST was performed after informing the patients about the study with brief explanation of possible results of the test. The Mantoux technique was used and two units of Purified Protein Derivative (PPD RT23, Staten Serum Institute, Copenhagen, Denmark) (kept in refrigerator and out of light at Chest and respiratory disease institute), were applied by an intradermal injection in the middle third of the inner forearm. Skin reaction was quantified 48 to 72 hours after the injection. Using transparent ruler, the largest transverse diameter of indurations was measured in millimeters. Patients who did not complete the test were excluded from the study. Only patients with positive TST were sent for chest radiography.

Results

A total of 166 patients were included in the study, 33 patients (19%) didn't complete TST and have been excluded.

Using cutoff point of ≥ 10 mm induration, a positive tuberculin skin test result was observed in 13 patients (9.8%). Table 1 shows distribution of study population according to tuberculin skin test results and personal characteristics. Among TST positive group, six patients (46.2%) had spent some time in prison, whereas only three patients (2.5%) of TST negative group reported such story. According to this study, history of incarceration was the only personal factor associated with statistically significant tuberculin reactivity ($P < 0.05$).

Table 2 highlights distribution of the study population according to tuberculin skin test results and medical history.

Table 1: Distribution of the study population according to tuberculin skin test results and personal characteristics.

Variables	Tuberculin Skin Test				P value
	Positive N=13		Negative N=120		
Gender					0.232
• Male	8	13.2%	53	86.8%	
• Female	5	6.9%	67	93.1%	
Age Group (year)					0.248
• 15-45	2	4.2%	45	95.8%	
• 46-65	8	13.3%	52	86.7%	
• > 65	3	11.5%	23	88.5%	
Job					0.619
• Housewife	5	7.4%	63	92.6%	
• Retired	2	13.3%	13	86.7%	
• Self-employee	6	15.8%	32	84.2%	
• Governmental employee	0	0.0%	6	100%	
• Military	0	0.0%	2	100%	
• Student	0	0.0%	4	100%	
Smoking Status					0.951
• Smoker	3	11.1%	24	88.9%	
• Ex-smoker	2	10.5%	17	89.5%	
• Non-smoker	8	9.2%	79	90.8%	
Family Size					0.535
• ≤ 7 persons	5	8.1%	57	91.9%	
• > 7 persons	8	11.3%	63	88.7%	
Spent any time in prison	6	66.7%	3	33.3%	**< 0.001**
Time before questioning					0.571
• ≤10 year	1	50%	1	50%	
• > 10 year	5	71.4%	2	28.6%	
Duration of incarceration					0.464
• ≤ 1 year	3	50.0%	3	50%	
• > 1 year	3	100%	0	0.0%	

Table 2: Distribution of the study population according to tuberculin skin test results and medical history.

Variables	Tuberculin Skin Test				P value
	Positive N=13		Negative N=120		
History of Contact to TB Patient	0	0.0%	4	100%	0.504
Previous history of TB	1	25%	3	75%	0.298
Use of Corticosteroids	0	0.0%	18	100%	0.133
Use of Immunosuppressive/Cytotoxics	0	0.0%	12	100%	0.232
History of Malignancy	0	0.0%	2	100%	0.639
Diabetes mellitus	4	8.9%	41	91.1%	0.806
Chronic Kidney Disease	3	9.7%	28	90.3%	0.983
Fever	0	0.0%	14	100%	0.193
Chronic liver disease	1	8.3%	11	91.7%	0.860
Heart failure	0	0.0%	11	100%	0.254
Stroke	2	33.3%	4	66.7%	**0.047***
Systemic lupus erythematosus	0	0.0%	5	100%	0.453
Upper GI bleeding	1	20%	4	80%	0.433
COPD	1	33.3%	2	66.7%	0.165
Deep venous thrombosis	0	0.0%	3	100%	0.564
Miscellaneous	4	14.8%	23	85.2%	0.232

* Patients with stroke and TST positive result have another risk factor, i.e., history of incarceration, which could explain this association.

Discussion

The current study found that 9.8% of hospitalized patients in a single medical unit in a specified period to be TST positive. In Iraq there is no recent data regarding prevalence of latent tuberculosis in the community. In the 1960s, TST was found to be positive in 17% and 30% of rural and urban population, respectively[11]. In 2008, a study conducted in the same hospital, revealed that the rate of tuberculin reactivity among health care workers is about 25%, the positivity correlated well with the duration of employment, reached 44% among ward nursing staff who have been employed for more than 10 years[11].

In comparison with previous studies and with a prevalence of tuberculosis of about 73 /100000 population, it was expected to find higher percentage of tuberculin positivity in the current study. This low level of tuberculin positivity may be related to the compromised health of hospitalized

patients with their impaired immune response. In these patients, two-step test may booster their immune response with resultant higher rate of positivity. Also, it is well known that even among patients with proven tuberculosis and no apparent immunosuppression, 10 to 20 percent will have negative results on tuberculin skin tests[12], furthermore, we performed TST using tuberculin dose of two units. Other possible explanation is a decline in the burden of disease with ongoing TB control program in the country.

The main risk factor for tuberculin positivity in the study was history of incarceration, a point well known to increase susceptibility for acquiring *M. tuberculosis* infection. As prisoners are at higher risk of being infected with tuberculosis than is the general population and the conditions of the prison environment can facilitate the dissemination of tuberculosis due to overcrowding, poor nutrition and poor ventilation[13]. This finding corroborates the results observed in several other studies regarding the prevalence of active and latent tuberculosis in prison facilities which is higher than that found in the community. The prevalence of latent tuberculosis infection had ranged between 45% among prisoners in Lebanon (13) and 87% among prisoners in a study from Malaysia[14].

Other studies had found increasing prevalence of latent TB with age[15-17] and higher level among males in comparison with females[18-20], no significance association was found in the current study.

Patients with latent TB are the reservoir of TB bacilli in the community. In the first phase to control tuberculosis, detection and treatment of cases with active disease are priority, but to eradicate the disease we need to prevent the occurrence of new cases and this is done by eradication of latent infection. In the United States, the Public Health Service already recommends screening and treatment of persons at increased risk for latent tuberculosis as the critical strategy for elimination of tuberculosis in the country[8]. Patients with latent infection have a 5% lifelong risk of development of active disease[7], while patients with suppressed immunity have even higher risk which in HIV-infected patients may reach up to 25% per annum[6]. In countries with low prevalence of tuberculosis, it is recommended to treat these patients as treatment reduces the risk of development of active disease by about 90%[7]. In countries with high prevalence the situation may be different, the patient will remain susceptible for exposure to bacilli in the community and possibly acquiring the infection again. A recent study from South Africa stated that mass screening and treatment for latent tuberculosis had no significant effect on tuberculosis control in South African gold mines, despite the successful use of isoniazid in preventing tuberculosis during treatment. One contributory factor that was suggested by the authors is the high burden of the disease in that community with ongoing transmission of tuberculosis and the exposure of the patients to reinfection[21]. An analysis from a trial conducted in Uganda showed that isoniazid therapy initially protected against the development of tuberculosis in tuberculin-positive HIV-infected persons, but its benefit was lost one year after beginning of treatment[12]. The situation differs from country to another, these African studies cannot answer the question to treat or not to treat patients in our country with latent infection who have underlying immunosuppressive diseases such as diabetes mellitus or chronic renal disease. Studies with long follow up are needed to compare treatment with observation. For the time being, knowing the TST result can alert the physician for early investigation and treatment if the patient has develop clinical features compatible with tuberculosis. Furthermore, knowing the magnitude of latent TB is important for future eradication plane of the illness.

In conclusion, the overall frequency of tuberculin skin test positivity was 9.8% in the study population. History of incarceration is the only factor associated with significant tuberculin reactivity among

hospitalized patients in a single medical unit in Baghdad teaching hospital.

Population based study is needed to determine the prevalence of latent tuberculosis in the community. Studies with long follow up are needed to determine the value of treating latent tuberculosis in patients with underlying immunosuppressive diseases such as diabetes mellitus and chronic kidney disease.

References

1. *Golchin M, Rostami M.* Tuberculin test in nursing and human-sciences students. JRMS 2005; 10(3): 172-6.
2. Raviglione M, O'Brien R. Tuberculosis. In: Longo DL, Fauci SA, Kasper DL et al (Eds.). Harrison's Principles of Internal Medicine. 18th ed. USA: McGraw-Hill Medical 2012. P 1340-59.
3. Zumla A, Raviglione M. Tuberculosis. N Eng J Med 2013;368:745-55.
4. National tuberculosis programme - Iraq [Internet]. [cited 2014 Feb 8]. Available from: http://ntpiraq.zaghost.com/ntpoverview.htm
5. Iraqi ministry of health. The quarter report for recorded TB cases according to age and sex in Iraqi governorate 2012.
6. Kasprowicz V, Churchyard G. Diagnosing latent tuberculosis in high-risk individuals: rising to the challenge in high-burden areas. J Infect Dis 2011; 204:S1168-78.
7. Chee C, Sester M. Diagnosis and treatment of latent infection with *Mycobacterium tuberculosis*. Respirology 2013;18:205-16.
8. Horsburgh C, Rubin E. Latent tuberculosis infection in the United States. New Engl J Med 2011;364:1441-48.
9. Wang L, Turner M. A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. Thorax 2002;57:804-9.
10. Balcells M, Pe´rez C. A comparative study of two different methods for the detection of latent tuberculosis in HIV-positive individuals in Chile. Int J Infect Dis 2008; 12: 645-52.
11. Radi Ali A. Rate of tuberculin reactivity in health care workers, Baghdad teaching hospital. Iraqi Board for Medical Specializations, Internal Medicine; 2008.
12. Jasmer R, Nahid P. Latent tuberculosis infection. New Engl J Med 2002;347:1860-66.
13. Hussain H, Akhtar S. Prevalence of and risk factors associated with *Mycobacterium tuberculosis* infection in prisoners, North West Frontier Province, Pakistan. Int J Epidemiol 2003;32:794-9.
14. Margolis B, Al-Darraji H. Prevalance of tuberculosis symptoms and latent tuberculous infection among prisoners in northeastern Malaysia. Int J Tuberc Lung Dis 2013;17(12):1538-44.
15. Li J, Munsif S. Prevalence of Tuberculin skin test positivity in clinical population in New York City. J Immigr Minor Health 2010;12:816-22.
16. D'Amelio R, Stroffolini T, Biselli R. et al. Tuberculin skin reactivity in Italian military recruits tested in 1996–1997. Eur J Clin Microbiol Infect Dis 2000;19: 200-4.
17. Bennett D, Courval J, Onorato I et al. Prevalence of tuberculosis infection in the United States population. Am J Respir Crit Care Med 2008;177: 348-55.
18. Holmes C, Hausler H. A review of sex differences in the epidemiology of tuberculosis. Int J Tuberc Lung Dis 1989;2(2):96-104.
19. Rhines A. The role of sex differences in the prevalence and transmission of tuberculosis. Tuberculosis 2013;93:104-7.
20. Diwan V, Thorson A. Sex, gender and tuberculosis. Lancet 1999;353:1000-01.
21. Churchyard G, Fielding K, Lewis J et al. A trial of mass isoniazid preventive therapy for tuberculosis control. Engl J Med 2014;370:301-10.

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