Prevalence of Latent Tuberculosis in End Stage Renal Disease Patients at Baghdad Teaching Hospital

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ABSTRACT:

BACKGROUND:

Tuberculosis (TB) is one of the oldest diseases known to affect humans, it caused by infection with Mycobacterium Tuberculosis (MTB). MTB is most commonly transmitted from a patient with infectious pulmonary TB to other person by droplet nuclei. End Stage Renal Disease (ESRD) patients are exposed to a variety of infections, including TB. The standard test for detecting Latent TB infection (LTBI) is tuberculin skin test (TST).

OBJECTIVE:

Determination the prevalence of latent tuberculosis among end stage renal disease patients in hemodialysis unit in Baghdad teaching hospital, and assessing its correlations with various conditions.

METHODS:

A stratified random sampling technique was used to select a sample of 71 patients of ESRD in hemodiaylsis unit in Baghdad teaching hospital. The selected patients were interviewed using a structured pretested questionnaire.

Two units of PPD (0.1mL) had been injected intradermally to the volar surface of forearm to be seen within 48-72 hours. The test was considered positive if (>=10mm induration) developed.

RESULTS:

The study showed the rate of tuberculin reactivity among End Stage Renal Disease (ESRD) patients is 28.57%. About 57.14% of patients were male; mean age of patient was 54.34 ± 15.25 years. The major cause of renal impairment were diabetes mellitus (DM) 52.86%, followed by hypertension 15.71%, duration of dialysis more than 6 months was 46.67% .

History of contact with active tuberculosis patient was 62.5%.

CONCLUSION:

Significant relationship between history of contact with active TB patients, duration of dialysis, and age of patients with TST positivity.

KEYWORDS: tuberculine skin test**,** end stage renal disease.

INTRODUCTION:

Tuberculosis is one of the oldest diseases known to affect humans; it is a major cause of death worldwide. This disease, which is caused by bacteria of the *Mycobacterium tuberculosis* complex, usually affects the lungs, although other organs are involved in up to one-third of cases. If properly treated, tuberculosis caused by drug-susceptible strains is curable in virtually all cases. If untreated, the disease may be fatal within years in 50–65% of cases MTB is most commonly transmitted from a patient with infectious pulmonary TB to other persons by droplet nuclei which are aerosolized by coughing, sneezing or speaking. The tiny droplets dry rapidly; the smallest one (<10 micron in diameter) may remain suspended in the air for several hours and may gain direct access `such as skin and trans - placental routes are uncommon and has no epidemiological significance. (1)

The initial infection usually goes unnoticed. Early lung lesions commonly heal, leaving no residual changes except occasional pulmonary or tracheobronchial lymph node calcifications. About 10% of those initially infected will eventually develop active disease, half of them during the first 2 years following infection; 90% of untreated infected individuals will never develop active TB. Appropriate completion of treatment for latent TB infection (LTBI) can considerably reduce the lifetime risk of clinical

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tuberculosis (TB disease) and is effective in persons with HIV infection. [2]

Latent tuberculosis infection is defined by the presence of an M. tuberculosis specific immune response in the absence of clinical and radiological disease. During latent infection, the host immune system is able to contain the bacilli in a state of non-replicating persistence[3,4]. It has been proposed that there is a spectrum of latent infection ranging from those with obvious TB lesions containing live bacilli but without symptoms (near active" TB) to those who have eradicated the infection with virtually no chance of reactivation.[5]

Several host factors, including age of less than 5 years, HIV co-infection, diabetes mellitus, smoking, under nutrition, chronic renal failure, and iatrogenic immunosuppression, increase the risk of progression to active TB in remotely infected individuals to levels much higher than 5% over several decades [6].

Contained latent infection reduces the risk of re-infection on repeated exposure, where as active tuberculosis is associated with an increased risk of second episode of tuberculosis on re-exposure [7].

Patients with ESRD undergoing chronic dialysis are much more prone to develop tuberculosis (TB) than the general population. In these patients, the diagnosis of TB disease is often difficult because of prevailing extra-pulmonary involvement and nonspecific symptoms[8].

The prevalence of latent TB infection (LTBI) in ESRD patients is elevated, and those who become infected are at high risk of developing active disease. Therefore, screening for LTBI in this population is recommended aiming to prevent progression to active TB and secondary contamination of others[9]. The tuberculin skin test (TST), the classic diagnostic tool for LTBI, has several major drawbacks, including poor sensitivity (because of a high prevalence of anergy in dialysis patients) and specificity with [false-positive tests in those vaccinated with bacilli Calmette–Gue´rin(BCG)]. The new immunological tests using IFN gamma release assays (IGRAs) have become available and have shown superior sensitivity and specificity for the diagnosis of TB compared with the TST in several studies, some very recent ones including ESRD patients.[8,9,10]

AIM OF STUDY:

- determining the prevalence of latent TB infection among ESRD patients admitted to hemodialysis unit in Baghdad teaching hospital, Medical city.
- assessing its correlations with various conditions.

PATIENTS AND METHODS:

Study design, setting and timing:

This was hemodialysis patients based cross-sectional study at negative machine in hemodialysis units in Baghdad teaching hospital from 1st of April to 15th of December 2014.

Sampling and patients:

Seventy one patients with ESRD on HD participated in our study. Twenty of them were positive Tuberculin test and sent for CXR, only one was abnormal CXR finding therefore excluded from the study, data collection about (age, history of contact with TB patient, history of smoking, causes of ESRD, duration of hemodialysis, history of TB, history of vaccination, and history of immune-suppressant therapy) were collected from participants as required.

Exclusion criteria:

Persons with active TB, history of pulmonary TB disease, immunosuppression and those who had received prior immunosuppressive therapy or hepatitis B&C were excluded from this study.

Study instruments:

Structured questionnaire consist of medical history including causes of ESRD, smoking habit, history of contact with TB patient, BCG vaccine, duration of hemodialysis, and history of TB. The TST was performed after informing the patient about the study with brief explanation of possible results of the test .The mantonx technique was used 2 units purified protein derivative (PPD RT23, staten serum institute, Copenhagen, Denmark) (kept in refrigerator and out of light at chest and respiratory disease institute) where applied by an intradermal injection in the middle third of inner forearm. Skin reaction was quantified 48 to 72 hours after the injection, using transparent ruler the largest transverse diameter of induration was measured in millimeters. Patient who did not complete the test were excluded from the study, only patient with positive TST were sent for chest radiography. If no induration, developed consider as (0mm). If induration develop, it was reported as (≥10mm) considered as positive TST.

Data Analysis

Statistical analysis was carried out using SPSS version 20.Categorical variables were presented as frequencies and percentages. Pearson‟s chi square (X2) test and fisher exact test were used to find the association between the categorical variables. A p-value of ≤ 0.05 was considered as significant.

RESULT:

Table 1: Basic characteristics of patients.

Variable		TST				P-VALUE	OR (95%CI)
		Postive		Negative			
		No.	%	No	%		
causes of esrd	DM	11	29.73	26	70.27	0.92	NA
	HT	3	27.27	8	72.73		
	OTHERS	6	27.27	16	72.73		
history of smoking	NO	14	28	36	72	0.867*	1.1(0.35-15.3)
	YES	6	30	14	70		
duration of dialysis		6	15	34	85	0.007*	4.9(1.6-15.3)
		14	46.67	16	53.33		
history of contact with tb patients	NO	15	24.19	47	75.81	0.038*	5.2(1.1-24.5)
	YES	5	62.5	3	37.5		
*fisher exact test							

* Smoker and current smoker

About 57.14% of patients were male; mean age was 54.34 ± 15.25 years. The major cause of disease was DM 52.9%, followed by hypertension 15.71%, median duration of dialysis 5 months.

Table 2: Relationship between TST and other variables.

Variable		TST				P-value	OR (95%CI)
		Postive		Negative			
		No.	%	No	%		
causes of esrd	DM	11	29.73	26	70.27	0.92	NA
	HT	3	27.27	8	72.73		
	others	6	27.27	16	72.73		
history of smoking	no	14	28	36	72	0.867*	1.1(0.35-15.3)
	yes	6	30	14	70		
duration of dialysis	less than 6 m	6	15	34	85	0.007*	4.9(1.6-15.3)
	more than 6 m	14	46.67	16	53.33		
history of contact with tb patients	no	15	24.19	47	75.81	0.038*	5.2(1.1-24.5)
	yes	5	62.5	3	37.5		
*fisher exact test							

Table 3: Effect of age on TST.

Variable		female		male	
		No.	%	No.	%
Causes of ERDS	DM	17	58.62	12	41.38
	HT	3	27.27	8	72.73
	OTHORS	10	33.33	20	66.67
History of contact with TB patients	Negative	26	41.94	36	58.06
	Positive	4	50	4	50
TST	Negative	20	40	30	60
	Positive	10	50	10	50
Age mean= SD		55.7=14.7		53.3=15.8	

Table 4: Gender adjusted baseline characteristics

Variable	TST		P value	OR(95%CI)
	positive No.=20	negative No.=50		
Age(years)	61.7=10.8	51.4=15.9	0.003	1.057(1.011-1.106)

DISCUSSION:

In our study the prevalence of LTBI among HD patients was (28.57%) in comparison with many studies that showed concordant with study in Brazil[19] was 28.5% in the first testing for TST and discordant with other studies that showed high prevalence of LTBI among HD patients 34% in Turkey[20] ,43.5% in Iran[21], and 53.9% in Taiwan[22], and this could be firstly due to high incidence of TB in their countries or poor TB control program and increase non MTB infection, secondly there is no booster testing was performed for TST in our study, this booster effect which increase in rate of positivity TST after one or two booster injections has been reported [19,23,24] . Thirdly BCG vaccination was found to have no effect on tuberculin reactivity in our study as in table (1), its well known that the effect of BCG vaccination on tuberculin test rarely exceed 10 years[25]. BCG in our country is usually done in the first week of life.

In other hand latent TB inSwitazarland19 %[26] and Saudia Arabia 19% [27] and 13% [28], this might due to good TB control program, adequate hemodialysis and good nutritional status of patients.

Our patients lower socio-economic state, start dialysis late, use less erythropoietin and are generally malnourished, found a direct correlation between dietary protein intake and cutaneous reactivity[29] .

In table (2) there is statistical significant association between TST positivity cases and duration of HD which is disagree from other studies[24,30] which is no statistical significant correlation because longer duration of dialysis has been correlated with worse cellular immunity Also in our study, there is statistical significant elevation of TST positivity increase with age as in table (3), which may represent an increase risk of reactivation of latent MTB infection with age [31, 32], concordant with other studies had found increase prevalence of LTBI with age [33,34,35] and discordant from study in Taiwan which no effect of age on latent MTB infection[22] because older people lived in a time when TB was much more prevalent than in later generations. The Percentage of LTBI is higher in patients with previous contact with active TB which showed in table (2) and this concordant with study in Campo Grande, state of mato Grosso do sul[36] in Brazil. HIV is the greatest risk factor for progression of recent or latent tuberculosis infection (LTBI) to active tuberculosis (TB) disease, in our study all patients were HIV sero-negative.

There is no statistical significant correlation between TST positivity and gender as showed in table (4) which is differed from other studies which showed males more TST positivity than females. [39]

CONCLUSION:

- In our study the prevalence of LTBI among End Stage Renal Disease patients were low (28.57%).

● there is significant relationship between history of contact with active TB patients, duration of dialysis, and age of patients with positivity of TST.

Recommendations:

● Tuberculin skin testing at start of hemodialysis and regular follow up after that is important step to prevent active TB in them.

● Future studies should be measure the TST positive in Iraqi general population in order to compare with current study.

●Future studies should be measure the TST positive and comparison with interferon gamma release assay in ESRD patients.

REFERENCES:

1. Dennis L.Kasper, Anthony S.Fauci, Dan L. Longo, Eugene B., Stephen I. Hauser, J. Larry Jameson. Marioc. Raviglione, Richard J.O‟Brien . Tuberculosis : Harrison's Principles of Internal Medicine. 16thMcgraw – Hill; 2005: 953.
2. David L. Heymann: Control of Communicable Diseases Manual18thEdition. An official report of the American Public Health Association 2008:607.
3. Dye C. Tuberculosis and lung disease 2000-2010 control but not elimination, International Journal of tuberculosis and lung disease2000; 4:146.
4. Aied Mohan; tuberculosis Infection rate in Iraq; Ministry of health (M.O.H) Iraqi guidelines of national program for tuberculosis eradication 1998:2-5.
5. Chee C, Sester M. Diagnosis and treatment of latent infection with Mycobacterium tuberculosis. Respirology 2013;18:205-16.
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. Zumla A, Raviglione M. Tuberculosis. New England Journal of Med. 2013;368:745-55.
8. LiviuSegall and Adrian cavic nephrology depertment, university of medicine and Pharmacy GT.PopaLasi,Romania. Diagnosis of TB in dialysis patient current strategy.
9. Thomas E. Rogerson, BSc,1,2 Sharon Chen, MBBS, PhD,3 Jen Kok, MBBS,3 Kamal Sud, MBBS,3 Kathy Kable, BASci, MN,3 and Angela C. Webster, MBBS, MM(ClinEpid), PhD1 Andrew Hayen,
10. BA, MM(Biostat), PhD,2 Jonathan C. Craig, MBBS, PhD,1,2.Tests for Latent Tuberculosis in People With ESRD.
11. Horsburgh C, Rubin E. Latent tuberculosis infection in united States. New Engl J Med 2011;364:1441-48.
12. American Thoracic society. Targeted tuberculin testing and treatment of latent tuberculosis infection.American Journal of respiratory and critical care Med. 2000;161:S221-47.
13. Aerts A, Habouzit M, Mschiladze L, et al. Pulmonary Tuberculosis in prisons of the Ex-USSR State of Georgia: Result of a nation-wide prevalence survey among Sentenced Inmates. International Journal of Tuberculosis and Lung Disease.2000;4:1104-10.
14. Robet M. Jasmer, Payam N, and Philip C. Hopewell; Latent Tuberculosis Infection, N. Engl. J. Med. 2002;347:1860-65.
15. 1Sonal M, Diana N, Felicia D. Guidelines for testing and treatment of latent tuberculosis infection. NYC department of health and mental hygiene.Burean of tuberculosis control. 2005: 4-13.
16. Division of tuberculosis elimination (DTBE). CDC fact sheets; tuberculin skin testing. 2007: 1-2.
17. Helena J. Chapman and Michael Lauzardo MD msc. Advance in diagnosis and treatment of latent TB infection (JABFIM).
18. Timothy R. Sterling, David W.Hass. Transmission of Mycobacterium tuberculosis from health care workers. Engl. J. Med.2006;355:119-20.
19. Radi Ali A. Rate of tuberculin reactivity in health care workers, Baghdad teaching hospital. Iraqi board for medical specializations, internal medicine; 2008.
20. Fonseca JC, Caiaffa WT, Abreu MN, Farah Kde P, CarvalnoWda S,Spindlo De Miranda S. Prevalence of latent TB infection and risk of infection in patients with chronic kidney disease undergoing HD in a referral center in Barazil. J Bras Pneumol. 2013;39: 214-20.
21. Seyhan EL, Sokucu S, Altin S, Gunluoqlu G, Trabtus S, Yilmas D, Kaksalan OK, Issever I . Comparison of the quantiferon-TB Gold in – tube test with tuberculin skin test for detecting latent tuberculosis infection in haemodialysis patients.Transpl. Infect. Dis. 2010;12:98-105; doi: 10.1111/. 1399-3062. 2009 . 00469.x. Epubo 2009 Nov 10.

22. Savai S, SavoiJ, Ranibar M, SabzqhabaeiF . Interferon-gama release assay agreement with tuberculin skin test in pretransplant screening for latent TB in high prevalence country. Iran J kidney disease 2014;8:329-32.

23. Lee SS, Chou KJ, Dou HY, Huang TS, Ni YY, Fang HC, SY CL, Chen JK, Wang YH, Lin HH, Chep YS .High prevalence of latent TB infection in dialysis patients using the interferon-gamma release assay and tuberculin skin test. Clin. J AM SOC Nephrol. 2010;5:1451-7;doi: 10.2215/CJN. 01796. Epub 2010 Jun 10.

24. Aqorwal SK, Gupta S, Bhowmik D, Mahajan S .Tubercline skin test for the diagnosis of latent TB during renal replacement therapy in an endemic area: single center study. Indian J Nephrol 2010;20:132-6;doi : 10.4103/ 0971-4065. 70842.

25. Saqheb MM, Goodarzi M, RoozbehJ . The booster phenomenon of tubercline skin testing in patients receiving HD. Iran J. Immund 2008;5;212-6;doi;UIV 5i4A4.

26. Wang L, Turner MO, Elwood RK, Schulzer and Fitz Gerald. Ameta-analysis of the effect of BCG vaccination on tubercline skin test measurments; Thorax 2002: 804-9.

27. Triverio PA, Bridevaux PO, Ronx-lombard P, Niksic L, Rochat T, Martin PY, Sandan P, Janssens JP. Tuberculine skin test for detection

28. of latent tuberculosis in chronic haemodialysis patients.NephrolDial transplant 2009 ;24:1952-6. Doi: 10. 1093/ndf/gfn, 748.Epub 2009 Jan 22.

29. HoDa Abdel Hadi Hassan, Mahmoud Shorman, Abdel Rahman E.I. Housawi, and Mohamed Y. Elsammon.Detecting latent TB infection prior to kidney transplantation intertiary hospital in Saudi Arabia: Comparison of the T- Spot- TB test and tubercline test. British microbiology research journal 3(2) : 116-127, 2013.

30. Al-Jahadali H, Ahmed AE, Balkhy HH, Baharroon S, AL-Hejaili FF, Hajeer A, Memish Z, Binsaliah S, AL-Sayyari AA. Comarison of the tubercline skin test and Quanti-FERON-TB Gold in –tube (QFT-G) test for diagnpsis of latent TB infection in dialysis patients. J Infect Public health 2013;6:166-72;doi: 10. 1016/J.Jiph.2013.02.002 2013 Apr 23.

31. Akiyama M, numata A, Imagawa A. Influnce of protein intake on phytohemagglutin skin test in patients undergoing maintenaince hemodialysis. NippoaHinyokikaGakkaiZasshi. 1989; 80: 1175-1180.

32. Roya HABIBIAN, Ali MOMENI, Massoud AMIRI. Tubercline skin test, booster phenomenan and related changes in HD patients in Shahrekrd, Iran.Turk J Med Sci(2014) 44: © TUBITAK dol: 10/3906/sag-1308-93.

33. Bllien EY, Fletcher DD, Safyer SM . Association of tuberculosis infection with increase time in admission to the New York city jail system. JAMA 1993;269: 2228-31.

34. Scholten JN, Fujwara PI, Frieden TR . Pervalence and factors associated with tuberculosis among new school entrants, New York city 1991-1993. Int J Tuberc. Lung dis. 1999;3:31-41.

35. Li J, MunsifS.prevalence of tubercline skin test test positivity in clinical population in New York city. J Immigr Minor Health 2010;12:816-22.

36. D'Amelio R, Stroffolini T, Biselli R et al. Tuberculin skin reactivity in Italian military recruits tested in 1996-1997, Eur J ClinMicrobiol infect Dis 2000;19:200-204.

37. Bennett D. Courval J, Onorato I, et al. Prevalance of tuberculosis infection in the united state population. Am J Respir Crit Care Med 2008;177: 348-55.

38. Chagas AC, Hans Filho G, De oliveira SM, IVO ML, Correa Filho RA, Donatti MI. Prevelance of latent TB and treatment adherence among patients with chronic kidney disease in campo Grand, state mato grosso do sul. Rev Soc Bras Med Trop. 2014;47: 204-11.

39. Selwyn P, Hartel D, Lewis V, Schoenbaum E, Vermund S, Klein R, Walker A, Friedland G. A prospective study of the risk of tuberculosis among intravenous drug users with human immunodeficiency virus infection. N Engl J Med. 1989;320:545–50. doi: 10.1056/NEJM198903023200901.

40. Allen S, Batungwanayo J, Kerlikowske K, Lifson A, Wolf W, Granich R, Taelman H, Van de Perre P, Serufilira A, Bogaerts J. Two-year incidence of tuberculosis in cohorts of HIV-infected and uninfected urban Rwandan women. Am Rev Respir Dis. 1992;146:1439-44. doi: 10.1164/ajrccm/146.6.1439.

41. Rao TM1, Ram R, Swarnalatha G, Santhosh Pai BH, Ramesh V, RAo CS, Dakshinamurty KV. Tuberculosis in haemdialysis patients: A single center experience. Indian J Nephrol. 2013;23: 340-5. doi: 10.4103/0971-4065.116296.