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CLINICAL STUDY

The Affecting Factors and Comparison of Tuberculin Skin Test in Peritoneal Dialysis and Hemodialysis Patients

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Abstract

Compared with the general population, patients with chronic renal failure have increased tuberculosis (TB) prevalence and mortality rates. In this study, we aimed to investigate tuberculin skin test (TST) positivity rates in hemodialysis (HD) and peritoneal dialysis (PD) patients and the factors influencing TST positivity. Ninety-two HD patients and 44 PD patients who had been on HD and PD treatment for at least 3 months were recruited into the study. TST was administered in all patients. Positivity was defined as an induration diameter >10 mm. At least 5 mm of induration following skin testing together with a chest radiography indicating previous infection was defined as latent TB infection. TST positivity rates, diameter of TST indurations, and serum albumin levels in HD patients were higher than the PD patients. TST induration size was not correlated with any other parameters in both HD and PD groups. TST-positive patients had higher albumin levels and lower leukocyte count than the TST-negative patients. In TST-positive patients, albumin level was correlated with the duration of dialysis but TST induration size was not correlated with the lymphocyte count and albumin level. In our study, TST positivity of patients was found in 30.4% of HD patients, 9% of PD patients, and 23.5% of total patients. It is still recommended to use TST for the screening test of TB. We found a significant relationship between TST and albumin level. It should be remembered that TST response may be lower in PD patients, especially in cases in which TB is suspected.

Keywords: chronic renal failure, hemodialysis, peritoneal dialysis, tuberculin skin test

INTRODUCTION

In developing countries, tuberculosis (TB) is an infectious disease that causes common morbidity and mortality and threatens public health. Patients having low socioeconomic conditions and impaired immunity (transplant, dialysis, HIV infection, etc.) have increased risk of developing TB and progression of the latent TB to active disease.^{1–3} Compared with the general population, patients with chronic renal failure (CRF) have increased TB prevalence and mortality rates.^{4–13} The main reason is the decreased T-cell function due to uremia and malnutrition. Vitamin D deficiency and hyperparathyroidism are the other factors that may contribute to the decreased cellular immunity.^{13–15}

CRF patients are also candidates for transplantation and in these patients, the diagnosis of TB is

becoming more and more important. In dialysis patients, TB diagnosis is more complex and difficult because of an increased frequency of extrapulmonary involvement, atypical presentation, and non-specific symptoms and findings.^{13,16–23} Tuberculin skin test (TST) has high false-negative rates in patients with end-stage renal disease.^{1,3,6} Anergy in the general population is below 5% but in CRF patients it is between 32% and 40%.^{3,13,24}

As expected, there is an increased risk of TB among hemodialysis (HD) and peritoneal dialysis (PD) patients in developing countries.²⁵ Turkey is one of the countries where the disease is endemic.²⁶ Latent TB infection is 52.5 times more likely to be reactivated in patients with renal failure compared with the general population,²⁷ so screening is necessary. It has also been noted that annual TST plus a routine chest radiograph improves detection of TB infection.¹⁸

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The limit of TST positivity in CRF patients has no precise standardization, and TST values exhibit great differences between endemic and epidemic areas. HD patients are exposed to hospital environment more often than the PD patients. Therefore, the risk of TB in these patients may be expected to be higher. In the literature, there is not much data regarding the rate of TST positivity in HD and PD patients. In this study, we aimed to investigate TST positivity rates in HD and PD patients and the factors influencing TST positivity.

PATIENTS AND METHOD

Ninety-two HD patients (54 males and 38 females) and 44 PD patients (25 males and 19 females) were recruited into the study. The mean age was 51.9 ± 15.5 years. These patients were on HD and PD treatment for at least 3 months. TCT was administered in all patients. Demographic information, laboratory tests, chest radiography results, and BCG (Bacille Calmette–Guerin) vaccination status were recorded. None of the patients had any active infection, ongoing connective tissue disease, or immune disorders. The etiologies of primary renal disease of the participants were as follows: chronic glomerulonephritis (14 subjects), diabetic nephropathy (41 subjects), hypertensive nephropathy (32 subjects), polycystic kidney disease (9 subjects), nephrolithiasis (5 subjects), others (7 subjects), and unknown etiology (28 subjects). The study protocol was approved by the local Hospital Ethics Committee and all the participants provided informed consent.

The patients received tuberculin test by using the Mantoux technique with 0.1 mL (5 tuberculin units) of purified protein derivative intradermally injected into the volar surface of the forearm that did not have the arteriovenous shunt. The investigator read the result of the TST 48–72 h later. Positivity was defined as an induration diameter >10 mm. At least 5 mm of induration following skin testing together with a chest radiography indicating previous infection was defined as latent TB infection.²⁸ Laboratory tests included *Kt/V*, serum albumin, hemoglobin (Hb), leukocyte count, lymphocyte count, parathormone (PTH), and phosphorus (P). Dialysis sufficiency was defined as *Kt/V* >1.2 for HD and >1.7 for PD subjects.^{29,30}

Statistical Analysis

SPSS 15.0 (SPSS, Inc., Chicago, IL, USA) was used for statistical analysis. Descriptive statistics include mean $\pm$ standard deviations for continuous variables and frequencies and proportions for categorical variables. Chi-square test was used to compare categorical variables. Continuous variables were compared using Student's *t*-test. A value of $p < 0.05$ was considered significant.

RESULTS

In this study, TST positivity of patients was found in 30.4% of HD patients, 9% of PD patients, and 23.5% of

Table 1. Demographic data of HD and PD patients.

	HD	PD	<i>p</i> -Value
Age (years)	54 ± 15.1	46.47 ± 15.0	0.004
Gender (M/F)	54/38	25/19	>0.05
Duration of dialysis (months)	43.9 ± 34.9	23.7 ± 17.9	0.001

Table 2. Comparison of laboratory data of patients with HD and PD.

	HD	PD	<i>p</i> -Value
<i>Kt/V</i> sufficient ^a	83.9%	66.3%	>0.05
Hemoglobin (g/dL)	10.99 ± 1.69	11.15 ± 1.82	>0.05
Leukocyte (hpf/ μ L)	7.06 ± 2.2	8.2 ± 2.4	0.008
Lymphocyte (hpf/ μ L)	2.2 ± 0.9	1.64 ± 0.66	0.001
PTH (pg/mL)	354.59 ± 296.03	459.10 ± 429.66	>0.05
P (mg/dL)	4.41 ± 1.31	4.80 ± 1.63	>0.05
Albumin (g/dL)	3.85 ± 0.42	3.05 ± 0.41	0.000
TST (mm)	8.56 ± 6.52	2.86 ± 4.82	0.000
TST ⁺ ^a	30.4%	9.0%	0.006
BCG ⁺ ^a	67.4%	90.9%	0.005

Note: ^aChi-square test was used.

total patients. Demographic data of HD and PD groups are summarized in Table 1. The patients in HD group were significantly older than in PD group and had a longer duration of dialysis. Laboratory data results of HD and PD groups were summarized in Table 2. Both groups did not differ with respect to adequacy of dialysis. Absolute leukocyte count was higher in PD patients and lymphocyte count was higher in HD patients. HD patients had significantly higher serum albumin levels than PD patients. Ratio of BCG vaccination was higher in the PD group. TST positivity and diameter of TST indurations in HD patients were significantly higher than in the PD patients. TST induration size was not correlated with any other parameters in both HD and PD groups. Albumin levels in HD patients had positive correlation with dialysis durations ($p = 0.006$, $r = 0.29$) and Hb levels ($p = 0.002$, $r = 0.32$). Lymphocyte count and *Kt/V* values did not correlate with any parameter. We found a significant negative correlation between albumin levels and the duration of PD ($p = 0.001$, $r = -0.5$).

The TST-positive and TST-negative patients were compared by age, duration of dialysis, *Kt/V* value, the number of lymphocytes, and the value of PTH and P; hence, the differences were not statistically significant (Table 3). TST-positive patients had significantly higher albumin levels and significantly lower leukocyte count. In TST-positive patients, albumin level was correlated with the duration of dialysis ($p = 0.03$, $r = 0.38$) but TST induration size was not correlated with the lymphocyte count and albumin level. In TST-negative patients, albumin was correlated with the duration of dialysis, lymphocyte count, and TST induration size

Table 3. Comparison of TST-positive and TST-negative patients (HD vs. PD).

	TST (+)	TST (-)	<i>p</i> -Value
Age (year)	51.56 ± 15.53	52.12 ± 15.58	>0.05
Duration of dialysis (months)	40.76 ± 32.01	36.64 ± 32.02	>0.05
BMI (kg/m ²)	24.66 ± 4.52	25.30 ± 5.77	>0.05
<i>Kt/V</i> sufficient	74.2%	83.3%	>0.05
Hemoglobin (g/dL)	10.87 ± 1.79	11.10 ± 1.71	>0.05
Lymphocyte count (hpf/μL)	1.98 ± 0.68	2.02 ± 0.98	>0.05
Leukocyte (hpf/μL)	6.62 ± 2.30	7.69 ± 2.37	0.02
PTH (pg/mL)	290.35 ± 300.45	417.99 ± 354.42	>0.05
Albumin (g/dL)	3.84 ± 0.46	3.52 ± 0.57	0.005
P (mg/dL)	4.33 ± 1.01	4.60 ± 1.53	>0.05

($p = 0.003$, $r = 0.29$; $p \leq 0.001$, $r = 0.35$; and $p < 0.001$, $r = 0.44$, respectively). In the TST-negative group, 61.5% of patients had HD and 38.5% had PD.

DISCUSSION

In this study, TST positivity of patients was found in 30.4% of HD patients, 9% of PD patients, and 23.5% of total patients. In several studies, TST positivity was found to be between 11% and 68% according to the region and center of study, patient characteristics, and the admission limit of positive test.^{18,23,31–33} In a prospective study of 200 renal transplanted patients, Agarwal et al.³⁴ reported that the risk of developing TB was found to be similar in patients with positive and negative TST and suggested that TST was not specific and sensitive in the diagnosis of TB. HD patients are more often exposed to the hospital environment and are usually older compared with the PD patients. For these reasons, it is expected that the HD patients are more likely to develop TB than the PD patients.

In this study, it is seen that the HD patients showed a stronger response (diameter of induration) to TST than the PD patients. In the HD patient group, the size of induration and number of patients with positive TST were significantly higher than in the PD group. The lymphocyte count and albumin level in HD patients were higher than in the PD patients. These results evoked us to consider that immune responses are stronger in HD patients due to higher levels of nutritional parameters, overall health status, serum albumin, and lymphocyte count. However, serum albumin level and lymphocyte count in both groups had no significant correlation with the diameter of TST indurations. Other possible causes might be that the HD patients were older and had frequent exposure to hospital environment than the PD patients. Cristopoulos et al.³⁵ reported that age of patients is a risk factor for TB. Although the frequency of vaccination with BCG in PD patients is higher than

in the HD patients, a stronger response to TST in HD patients suggests that T-cell functions are weaker in PD patients.

Considering all the patients, there was no correlation between BCG positivity rates and TST positivity rates. Contagion may be higher in HD treatment because the patients on HD treatment have frequent exposure to hospital and other patients on HD session.

In our study, the duration of HD was significantly correlated with the albumin levels but not correlated with the diameter of TST indurations. In PD patients, negative correlation was established between albumin levels and the duration of dialysis. This might be due to chronic peritoneal damage and peritoneal albumin loss. Peritoneal albumin loss may be a cause of low response to TST in PD patients. In both groups, no difference was detected in *Kt/V* values, measure of adequacy of dialysis, suggesting that there is no relationship between the dialysis adequacy and the response to TST.

In the regression analysis of our study, albumin, *Kt/V* value, lymphocyte count, body mass index, and other clinical and laboratory parameters had no effect on the frequency and response of TST. Wauters et al.¹⁷ also found similar results.

All patients with PD and HD groups were separated into TST-positive and TST-negative groups, and higher albumin levels and lower leukocyte counts were determined in TST-positive patients. There was no significant difference in the other laboratory parameters. Wauters et al.¹⁷ in 2004 reported that in HD patients the *Kt/V* values, nutrition, and albumin levels did not differ between TST-positive and TST-negative patient. Fang et al.²² in their study found 22% of their sample had anergy to TST, 15% of the anergic group had an active TB, and albumin levels were higher in this group. Habesoglu et al.³¹ reported that TST reactivity had a positive correlation with previous TB history and negative correlation with the serum ferritin. They did not determine any significant difference between TST-positive and TST-negative patients in terms of dialysis adequacy, nutritional status, laboratory findings, and vitamin D intake. Aydoğan et al.³⁶ studied HD and PD groups and reported no significant difference between TST-positive and TST-negative patients in terms of leukocyte count, Hb, and albumin level. In our study, TST reactivity was not correlated with laboratory and demographic variables in PD patients.

In a study of 30 PD patients, Taskapan et al.³² did not detect a correlation between age, duration of CAPD, presence of BCG to TST reactivity, and anergy. There are some studies reporting that high PTH levels decrease CD4+ cell population and reduce the ratio of CD4/CD8.^{37,38} We found in TST-negative group of HD patients that PTH values were significantly higher. Griveas et al.³⁹ showed that the elevated level of PTH seems to affect the lymphocyte function and is associated with changes in cellular immunity in the HD patient population.

CONCLUSION

In our study, as cellular immunity is low in CRF patients, poor response rate to TST was high. But it is still recommended to use TST for the screening test of TB. We found a significant relationship between TST and albumin level. It should be remembered that TST response may be lower in PD patients, especially in cases in which TB is suspected.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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