



ORIGINAL ARTICLE

Screening for Tuberculosis in Patients Living with HIV Under Our Clinic's Care

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Abstract

Introduction: Tuberculosis (TB) is a prevalent opportunistic infection among individuals afflicted with human immunodeficiency virus (HIV). HIV infection significantly heightens the risk of TB development, whereas TB, in turn, accelerates the progression of HIV. Among individuals living with HIV, TB remains the most frequently observed disease. Our study's aim is the evaluation of TB tests among HIV/ acquired immunodeficiency syndrome (AIDS) cases.

Methods: This study encompassed HIV/AIDS patients aged over 18 years. Tuberculin skin test (TST) and interferon-gamma release assay test (IGRA) results of the patients were evaluated retrospectively. Microsoft Excel and Chi-square test were used to analyze the data and the relationship between assessments.

Results: 109 patients underwent TST, with twenty of them displaying reactions of ≥ 5 mm. Ten patients received IGRA testing and two of them tested positive. Two patients who were confirmed to have active TB during the study exhibited negative TST results, with IGRA not being evaluated in these cases. Among the 22 patients found to be TST positive, TB prophylaxis was initiated. The mean CD4+ T lymphocyte count in patients with TST positivity was $500.4/\text{mm}^3$, whereas in patients with IGRA positivity, it was $497/\text{mm}^3$. Moreover, the mean CD4 + T lymphocyte count in patients with negative TST results was $444.1/\text{mm}^3$, and it was $392.2/\text{mm}^3$ in patients with negative IGRA results. No statistically significant correlation was observed between TST results and patients' CD4 + T lymphocyte counts and serum HIV-RNA levels.

Discussion and Conclusion: The evaluation of TST and IGRA data within the context of HIV-infected cases presents a crucial perspective on the management of TB in this population. Our findings, alongside relevant literature, contribute to a deeper understanding of TB diagnostics and co-infection dynamics among individuals living with HIV. TB remains the leading cause of HIV-related morbidity and mortality. Screening for TB is essential in newly diagnosed HIV-infected cases.

Keywords: Acquired immunodeficiency syndrome; human immunodeficiency virus; interferon-gamma release tests; tuberculin test; tuberculosis.

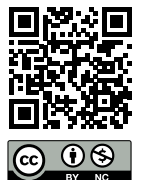
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Tuberculosis (TB) is an opportunistic infection commonly seen in individuals infected with the human immunodeficiency virus (HIV)^[1]. It can result from the progression of new infection or reactivation of latent infection and may manifest at any stage of HIV disease. HIV infection substantially increases the risk of developing TB, while TB, in turn, accelerates the progression of HIV infection, leading to the manifestation of acquired immunodeficiency syndrome (AIDS). The likelihood of developing active TB disease is increased by 50–110 times in HIV-positive individuals and is further escalated to 110–170 times in those with advanced AIDS. Notably, around one-third of the 36.7 million people worldwide living with HIV are estimated to have latent TB infection. TB remains the most common disease observed in individuals living with HIV, even among those undergoing antiretroviral therapy. Therefore, it is imperative to conduct HIV screening in every patient with suspected or diagnosed TB, as HIV-infected persons contribute significantly to the incidence of new TB cases. Furthermore, approximately one-third of HIV-related deaths are attributed to TB, making it the most frequent cause of mortality in HIV-infected individuals^[2,3].

This study aimed to evaluate TB diagnostic and screening tests, as well as the incidence of TB among HIV/AIDS cases.

Materials and Methods

The study included HIV/AIDS patients under the care and treatment of Haydarpaşa Numune Training and Research Hospital, specifically the Infectious Diseases and Clinical Microbiology Clinic. Patients older than 18 years with serologically confirmed diagnoses, whose medical files, special follow-up forms, and hospital information-processing system data were accessible, were included in the study. Tuberculin skin test (TST) was performed using the Mantoux method, administering a 0.1 mL dose of 5 tuberculin units of purified protein derivative into the hairless skin on the inner surface of the upper 2/3 of the left forearm, away from veins and skin lesions, using a single-use injector with a 27-gauge thick needle. Evaluation of the test was conducted at 72 h. As the interferon-gamma release assay tests (IGRA) could not be conducted at our hospital's laboratory, they were performed at the same center as recommended by the attending physicians during the relevant period.

Statistical Analyses

Data analysis involved calculating mean values using Microsoft Excel and using the Chi-square test to assess

relationships between TB screening tests and other measures.

Ethical approval was obtained from Haydarpaşa Numune Research and Training Hospital Ethics Committee with a registration date and number of January 27, 2017/HNEAH KAEK 2016/KK/121.

Results

Of the 200 patients meeting the inclusion criteria, 109 underwent TST, with twenty of them displaying TST reactions of ≥ 5 mm. In addition, ten patients received IGRA testing, and two of them tested positive. Intriguingly, two patients confirmed to have active TB during the study exhibited negative TST results, whereas IGRA was not evaluated in these cases. Both patients with positive IGRA results were male, aged 43 and 25 years, respectively, with CD4+ T lymphocyte levels of 420/mm³ and 574/mm³, and serum HIV-RNA levels of 31,000 IU/mL and 255,665 IU/mL, respectively. The first patient was classified as A2 according to the CDC classification, whereas the other was classified as A1. TST results were negative in both patients. Among the patients with negative IGRA results, 1 was female and 7 were male, with a mean age of 44.6. The mean CD4+ T lymphocyte count was 392.2/mm³, and the mean serum HIV-RNA level was 3,066,183 IU/mL. According to the CDC classification, 2 of the patients were classified as A1, 1 as B1, 2 as A2, 1 as A3, 1 as B3, and 1 as C3. TST was positive in 1 of these patients. Among the 20 patients with TST positivity, 2 were female and 18 were male, with a mean age of 38.5. The mean CD4+ T lymphocyte count was 500.4/mm³, and the mean serum HIV-RNA level was 5,655,044 IU/mL. According to the CDC classification, 8 of the patients were classified as A1, 2 as B1, 4 as A2, 4 as B2, and 2 as A3. Only 1 patient received IGRA testing, which yielded a negative result. Out of 89 patients with negative TST, 10 were female and 79 were male, with a mean age of 35.5. The mean CD4+ T lymphocyte count was 444.1/mm³, and the mean serum HIV-RNA level was 3,396,966 IU/mL. According to the CDC classification, 28 of the patients were classified as A1, 9 as B1, 1 as C1, 24 as A2, 10 as B2, 8 as A3, 6 as B3, and 3 as C3. TST was positive in 2 patients. No statistically significant correlation was found between TST/IGRA results and patients' CD4+ T lymphocyte counts and serum HIV-RNA levels. Detailed information of patients who tested positive for TST and IGRA is presented (Table 1).

Table 1. Findings of patients with positive TST and/or IGRA results

Number of Patients	Gender	Age	CD4+T lymphocyte count (/mm ³)	Serum HIV-RNA level (IU/mL)	CDC Classification	IGRA result	TST result (mm)
1	Male	43	420	31000	A2	Positive	1
2	Male	25	574	255665	A1	Positive	3
3	Male	36	467	1310000	A2	Negative	16
4	Male	59	550	204592	B1	-	20
5	Male	27	618	8410	A1	-	17
6	Male	29	325	925084	A2	-	8
7	Female	37	685	17327	A1	-	10
8	Female	32	381	22442	B2	-	8
9	Male	49	227	1487636	B2	-	10
10	Male	45	1018	9609	B1	-	21
11	Male	50	257	100000000	B2	-	10
12	Male	27	605	27368	A1	-	13
13	Male	19	627	147855	A1	-	14
14	Male	40	756	529899	A1	-	14
15	Male	26	169	422668	A3	-	8
16	Male	59	320	261591	A2	-	7
17	Male	34	376	2172070	B2	-	10
18	Male	51	679	1909077	A1	-	8
19	Male	38	765	1235326	A1	-	8
20	Male	38	174	507277	A3	-	12
21	Male	44	464	23357	A2	-	19
22	Male	30	545	1879288	A1	-	12

CDC: Centers for disease control and prevention; IGRA: Interferon-gamma release assay; TST: Tuberculin skin test.

Discussion

The evaluation of TST and IGRA data within the context of HIV-infected cases presents a crucial perspective on the management of TB in this population^[4]. Our findings, alongside relevant literature, contribute to a deeper understanding of TB diagnostics and co-infection dynamics among individuals living with HIV.

Contrary to our study, Çelikbas et al.^[5] reported negative TST results in a cohort of HIV-infected patients with active TB co-infection. This discrepancy might be attributed to variations in patient characteristics, such as immune status and TB strain virulence, which can influence TST outcomes. In our study, two patients with active pulmonary TB due to M. TB exhibited negative TST results. This emphasizes the challenges in solely relying on TST for TB diagnosis in HIV-positive patients and underscores the need for alternative approaches, such as IGRA, to enhance diagnostic accuracy. Our study stands as one of the few in our country presenting comprehensive TST and IGRA data for HIV/AIDS patients. The absence of large-scale studies in this area highlights the significance of our contribution to the existing literature. Further research with larger patient cohorts is

essential to validate and expand upon our findings, ultimately informing clinical practices and shaping diagnostic strategies.

The findings from this study reflect the heterogeneity of responses to TB diagnostic tests among HIV-infected patients. Both TST and IGRA demonstrated variability in their results, which can be attributed to differences in immunological responses and the underlying HIV-related immune suppression. This variability underscores the complex interplay between the two infections and the necessity of a multidimensional approach to diagnosis and patient management.

While our study provides valuable insights into TB screening in HIV-infected patients, there are limitations that warrant consideration. The lack of IGRA testing in our hospital's laboratory necessitated the performance of IGRA at an external center, potentially introducing variability in test conditions and interpretation. In addition, the limited number of patients who received IGRA hinders a comprehensive comparison between TST and IGRA in this cohort. Future studies should strive to address these limitations to provide more robust evidence.

Conclusion

The co-occurrence of TB and HIV infection remains a significant concern, with TB being a leading cause of mortality among HIV-infected individuals^[1,2,6,7]. Our study sheds light on the complexities of TB diagnostics in this population, emphasizing the need for a nuanced approach that considers both TST and IGRA results. The distinct responses observed in our study underscore the intricate immune interactions at play, highlighting the importance of individualized diagnostic and treatment strategies. While our study contributes valuable data to this field, further research on a larger scale is required to refine and validate these findings, ultimately improving the management of TB-HIV co-infection.

Ethics Committee Approval: Ethical approval was obtained from Haydarpaşa Numune Research and Training Hospital Ethics Committee with a registration date and number of January 27, 2017/HNEAH KAİK 2016/KK/121.

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Conflict of Interest: None declared.

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