J Renal Inj Prev. 2023; 12(2): e31994.

https://journalrip.com doi: 10.34172/jrip.2022.31994

Journal of Renal Injury Prevention

Assessment of the prevalence of latent tuberculosis infection in hemodialysis patients using tuberculin skin test

Azita Zafar Mohtashami[1], **Ali Amiri**[2*], **Babak Hadian**[1], **Pardis Nasiri**[3]

[1]Department of Internal Medicine, Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khorramabad, Iran
[2]Shahid Rahimi Hospital, Lorestan University of Medical Sciences, Khorramabad, Iran
[3]General Physician and Researcher, Lorestan University of Medical Sciences, Khorramabad, Iran

ARTICLE INFO

Article Type:
Original

Article History:
Received: 23 October 2021
Accepted: 19 December 2021
Published online: 8 January 2022

Keywords:
Tuberculin skin test
Interferon gamma release assays
Latent tuberculosis infection
Hemodialysis
Chronic kidney disease

ABSTRACT

Introduction: Patients undergoing dialysis are suffering from some degree of cellular immunity impairment which predispose them to develop latent tuberculosis infection (LTBI) which can turn into active tuberculosis (TB). Diagnosing LTBI in dialysis patients is helpful in preventing disease evolution.

Objectives: The aim of this study was to estimate the frequency of LTBI in a group of hemodialysis patients.

Patients and Methods: We studied all patients undergoing hemodialysis in Khorramabad teaching hospitals. Data were collected by completing a questionnaire through observation and interview. The Mantoux tuberculin skin test (TST) was performed, then 48 to 72 hours later, the induration was measured in millimeters. Results equal to or greater than 10 mm were considered positive.

Results: One hundred and nineteen patients undergoing hemodialysis participated in the study. The mean age of patients in this study was 58.55 ± 16.04 years. The induration size at the TST site was equal to or greater than 10 mm for 97 patients (81.5%) and less than 10 mm for 22 patients (18.5%). More than 81% of participants had LTBI. Until about two years later, none developed active tuberculosis without preventive treatment.

Conclusion: Several studies indicate the uncertainty of TST results in hemodialysis patients. Eighty-two percent positive is too much, and makes it difficult to consider all of them to be true positives. Therefore, it will be challenging to decide on starting preventive treatment. We recommend World Health Organization (WHO) to focus on a new affordable accessible efficient test for LTBI screening which does not require to be repeated or be confirmed by another diagnostic method, especially, for the expanded screening of the general population in the future.

Implication for health policy/practice/research/medical education:
Early detection of latent tuberculosis infection and initiation of preventive treatment for active tuberculosis infection especially in individuals with immune deficiency is crucial. A screening test should be able to differentiate between asymptomatic patients and healthy individuals. It seems necessary that the World Health Organization (WHO) seeks a cheap, fast, and reliable screening method.

Please cite this paper as: Zafar Mohtashami A, Amiri A, Hadian B, Nasiri P. Assessment of the prevalence of latent tuberculosis infection in hemodialysis patients using tuberculin skin test. J Renal Inj Prev. 2023; 12(3): e31994. doi: 10.34172/jrip.2022.31994.

Introduction

According to the World Health Organization (WHO), in 2019, about ten million people were infected with active tuberculosis (TB) and about 1.4 million deaths occurred from it (1). TB is caused by Mycobacterium TB with a significant incidence of morbidity and mortality, especially in people with impaired immune systems (2). About one-third of the world population has latent TB infection (LTBI), meaning they have TB bacteria in their body without any symptoms or signs of active TB (3). LTBI may become active TB over time. Patients infected with the human immunodeficiency virus (HIV),

***Corresponding author**: Ali Amiri, Email: Ali_pul_amiri@yahoo.com

transplant recipients and hemodialysis patients are more prone to develop active TB (4). The prevalence of chronic kidney disease (CKD) is estimated to be about 8 to 16% in the general population. CKD is associated with oxidative stress, inflammation, vitamin D deficiency, and malnutrition, all of which cause immune deficiencies (5). In patients with CKD, due to immunodeficiency status, a high frequency of infectious diseases and subsequent mortality is observed (6). Immune system deficiencies in patients with CKD, especially end-stage renal disease (ESRD) which requires dialysis, result from disorders in T cells and antigen presenting cells, and increased cytokines produced by monocytes (7-9).

According to immune system disorders, the incidence and prevalence of TB in patients undergoing dialysis is higher than the general population (10-12). Therefore, to prevent evolution of LTBI into active TB and its transmission to others, it is recommended to screen for LTBI in these patients (13).

Objectives

There are two common methods for diagnosing LTBI; the tuberculin skin test (TST) and interferon-gamma release assays (IGRAs) blood tests. Since the TST skin test is less sensitive and specific for LTBI and may be false positive in people who have been infected with non-tuberculous mycobacteria or have a history of Bacillus Calmette–Guérin (BCG) vaccination, IGRA blood tests are the preferred diagnostic method for patients receiving the BCG vaccine (14). We evaluated the prevalence of LTBI in hemodialysis patients in Khorramabad teaching hospitals, Lorestan province, Iran.

Patients and Methods

Study design

This study is cross-sectional study that was conducted in 2018. All eligible hemodialysis patients of the two dialysis centers of Lorestan university of medical sciences in Khorramabad participated. Inclusion criteria were age over 15 years and at least three months of dialysis. Exclusion criteria were patients being dialyzed for acute kidney injury and those with a history of known TB. Written informed consent was obtained from patients. Demographic data such as age, gender, education and place of residence and clinical diagnostic data according to the WHO guidelines on the management of LTBI were assessed and recorded in a questionnaire. Additionally, the proposed diagnostic algorithm for LTBI in the aforementioned guideline was considered as a basis for our practice (Figure 1) (15).

The size of induration reaction to TST at the injection site was also recorded. According to this algorithm, hemodialysis patients, which are considered an at-risk group, were first assessed for TB by taking history and physical examination for determined symptoms. Participants who had one or some of the TB clinical signs were further evaluated for TB according to the national guideline of TB in Iran, which mainly includes sputum smear investigation and chest X-ray. For others, a TST was performed to diagnose LTBI.

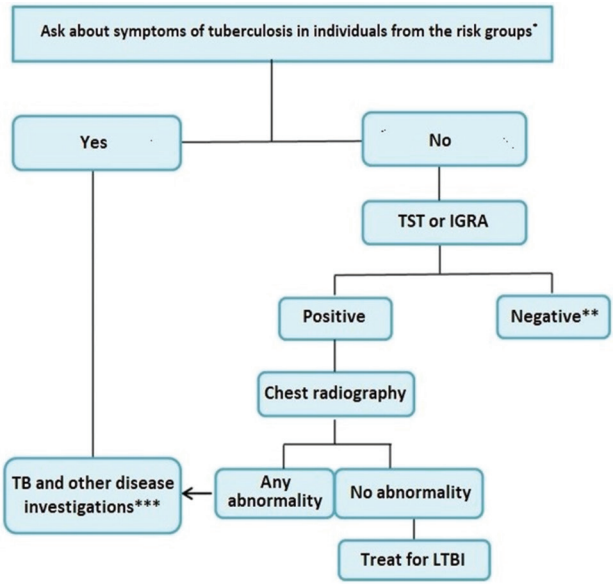

Figure 1. WHO algorithm for latent tuberculosis infection screening in high risk groups. *Any symptoms of TB include any one of: cough, hemoptysis, fever, night sweats, weight loss, chest pain, shortness of breath and fatigue. HIV test could be offered based on national or local guidelines or clinical judgment. Similarly chest radiographs can be conducted if efforts are intended also for active TB case finding. ** Clients for whom LTBI treatment is not indicated should be provided information about TB inducing the importance of seeking care if symptoms of TB developed. *** National TB guidelines should be followed while investigating for TB. In addition, those individuals in whom TB is excluded after investigations (inducing individuals with fibrotic radiologic lesions) can be considered for LTBI treatment.

For this test, 5 ml vials of human tuberculin purified protein derivative (PPD) manufactured by Razi vaccine and serum institute, Tehran, Iran were used. The expiration date of the vials was checked and the necessary cold chain was prepared. The TST was conducted by intradermal injection of 0.1 mL of PPD into the inner surface of the forearm by a professional vaccinator, then the injection site was marked. Forty-eight to 72 hours after injection, the indurated area was measured perpendicular to the length axis of forearm. Induration size equal to or greater than 10 mm was considered as positive (10). Fortunately, our study was concomitant with the routine periodical chest X-ray check-ups of patients.

Although evidence of abnormality was observed in chest X-rays for eight patients, none were in favor of TB. In other patients, the lung image was considered as normal. Chest X-rays were interpreted by both a radiologist and a pulmonologist concerning clinical signs.

Data analysis

Graphs and tables were used to show data distribution and summary measures for descriptive analysis. For comparing

groups with statistical tests, chi-square test was conducted for categorical (nominal) and *t* test for quantitative data. A statistical significance level of 0.05 was considered. SPSS version 18 software was used for statistical analysis.

Results

One hundred and nineteen eligible patients including 74 men (62.2%) and 45 women (37.8%) participated in the study. The patients had a mean age of 58.55 ± 16.04 years, a mean duration of dialysis of 37.66 ± 32.09 months and a hemodialysis schedule of three sessions per week on average. Eighty-one patients (68.1%) were diabetic and 84 patients (86.6%) were hypertensive. Two patients (1.6%) had hepatitis B. None had hepatitis C or HIV. Thirty-two of the participants were either currently or former smokers. None of the patients or his/her family had a history of TB. None of the patients had a history of TB or a family history of TB.

After an initial history taking and physical examination of the patients various symptoms such as cough, sputum, fever, night sweats were illustrated in (Table 1).

Then the symptomatic patients were then clinically examined by a pulmonologist who suspected seven of them as TB patients and referred for sputum smear test for TB bacillus and other necessary examinations. However, none of them was confirmed having TB.

According to the TST results, 97 patients (81.5%) with an induration equal to or greater than 10 mm were considered positive (Table 2). Mean of induration size for patients with positive results was 22.11 ± 12.51 mm and for all participants was 18.77 ± 13.97 mm.

After performing additional diagnostic tests in patients who had symptoms indicating TB and ruling out active TB, 97 hemodialysis patients (81.5%) were diagnosed as having LTBI (Figure 2).

The cases of LTBI and non-LTBI were compared in terms of other variables (such as gender, age, duration of dialysis, history of smoking, diabetes and hypertension). A statistically significant relationship was observed only between gender and LTBI, since it is more common in males than females in our study (Table 3).

Without any preventive treatment, none of the participants developed active TB until about two years after the end of the study.

Discussion

The aim of this study was to determine the frequency of LTBI in patients undergoing hemodialysis. In the study, the gender distribution of the patients was 74 (62.2%) male, which is almost the same as that for ESRD patients (16).

Studies show that LTBI diagnosed by either TST or IGRA can predict the development of active TB in dialysis patients (17) and therefore, requires preventive treatment (3). However, the relative risk of developing TB in dialysis patients with LTBI in comparison to those without LTBI is estimated to be about 1.49 (95% CI, 0.79; 2.80) for the TST test and about 2.03 (95% CI, 1.18; 3.50) for the IGRA test (15).

In our study, 81.5% of hemodialysis patients tested positive for TST, a very different result from most other studies. Anibarro et al evaluated the frequency of LTBI in 52 hemodialysis patients with TST and IGRA and reported 21.2% and 34.6% to be positive, respectively (18).

In 2010, Lee et al evaluated 93 patients with

Table 1. Absolute and relative frequency of signs and symptoms related to tuberculosis in participants

Clinical sign/ symptom	Yes		No	
	No.	Percent	No.	Percent
Cough	26	21.8	93	78.2
Fever	9	7.6	110	92.4
Sputum	16	13.4	103	86.6
Sweating	22	18.5	97	81.5
Loss of appetite	9	7.6	110	92.4
Weight loss	4	3.4	115	96.6
Chest pain	0	0.0	119	100
Shortness of breath	23	19.3	96	80.7

Table 2. The induration size of tuberculin skin test in hemodialysis patients

Induration size (mm)	Absolute frequency	Relative frequency
≥10	97	81.5
<10	22	18.5
Total	119	100

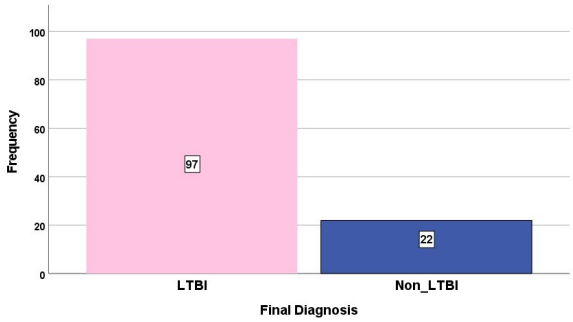

Figure 2. Frequency distribution of final diagnosis of LTBI in participants.

Table 3. Relationship between gender and final diagnosis

Final diagnosis	Gender		Total
	Male	Female	
LTBI	67	30	97
Non-LTBI*	7	15	22
Total	74	45	119

Pearson's chi-square = 10.584, df= 1, *P* value = 0.001, * Individuals without LTBI

QuantiFERON-TB Gold (QFT) and TST for LTBI in Taiwan and reported its prevalence using QFT as 34.4% positive and 10.8% intermediate, and with TST as 53.9% positive. About 64% of their patients were vaccinated with BCG (19). Of course, such percentages have not been observed in the study of Hussein et al in Egypt. In their study comparing IGRA and TST in active hemodialysis patients for LTBI in 2017, IGRA reported positive in 35.1% and TST in 13.5%. Based on these results, they concluded that in hemodialysis patients, LTBI cannot be easily ruled out with TST, and IGRA is recommended (20).

Madegedara et al in Sri Lanka investigated 77 CKD patients with TST and reported that about 27% of them had LTBI (21). In Taiwan in 2013, 2016, and 2020, the ESRD patients were examined for LTBI with IGRA blood test and the prevalence of LTBI was reported to be 25%, 20.5%, and 19.2%, respectively (22,23).

On the whole, in all of the aforementioned studies, the prevalence declared by both IGRA and TST test results were clearly different from our results. To be sure about the correct technique of performing TST, we employed a health professional with more than 15 years of experience in TST practice. All other necessary aspects regarding expiration date and maintaining cold chain for PPD vials were fully controlled.

The percentage of positive TST tests in our patients was much higher than in other studies, whether performed with TST or IGRA. TST is a valuable test but false positivity is of concern. In low-risk individuals, most positive reactions are, in fact, false positives due to the low-specificity of the TST test (24,25).

Numerous studies, including several systematic reviews, have been conducted to compare the TST and IGRA tests and nearly all of them acknowledge that the IGRA test has more sensitivity and specificity and is more reliable than the TST in diagnosing LTBI in dialysis patients and ESRD (26,27).

The Pasteur Institute of Iran started manufacturing the BCG vaccine in 1974 and vaccination of certain groups, including primary school students was begun. In 1988, the BCG vaccine was produced on a large scale in the country (28). More than half of the dialysis patients in our study also had a history of BCG vaccination. The debate over BCG vaccination and its impact on the TST test result has been going on for years. BCG vaccination may result in a false positive TST test for years (27-30).

The World Health Organization notes that if BCG is given at birth, it will have little effect on the specificity of the TST test. Therefore, it points out that BCG vaccination history should not be a determining factor in test selection (15). However, BCG administration after infancy or repeated administration causes more severe and larger TST reactions (31).

The results of several systematic reviews, including the 2008 study by Pai et al, and the 2011 study by Diel et al, and the guidelines of the US Centers for Disease Control and Prevention (CDC) suggest that in individuals with a history of BCG vaccination the TST may cause a false positive reaction, therefore IGRA is more specific and is the preferred test (32-37).

Another reason to use an IGRA test instead of a TST test in individuals with a history of BCG vaccination is to avoid the inappropriate administration of isoniazid (38). It is important to know even in confirmed LTBI cases, the effectiveness of existing drugs is about 60% to 90% (15). However, some studies indicate that the history of BCG vaccination does not have a significant effect on TST size (39).

Conclusion

The prevalence of LTBI and the risk of active TB is high in hemodialysis patients and it is necessary to make an effort to diagnose LTBI and apply a preventive treatment.

Most of the patients in our study who are TST positive may be infected with non-TB mycobacteria and/or have a history of BCG vaccination which may be false positives. Even we are not sure that the negative results are all true. Although WHO algorithm for LTBI screening has helped us to assure the participants who have not active TB, we are in doubt about the LTBI, while it is difficult to make a decision about preventive treatment of them.

Even though IGRA blood tests are more sensitive and specific than TST, their results are not absolutely reliable. Therefore, for achieving the global end TB goal, our recommendations are listed below;

In the future, we may need to expand LTBI screening to a larger population. In long-term strategic planning, it is suggested that World Health Organization attempts to set goals for innovating cheaper and more accessible diagnostic methods. More reliable tests that help health professionals to administer treatment with less doubt are necessary.

In WHO algorithm, TST and IGRA are assumed to be equal for screening LTBI in hemodialysis individuals. However several studies indicate low-specificity of TST and suggest the IGRA test to be as the preferred method. It is suggested to consider history of BCG vaccination in the algorithm and explain it as a determining factor in test selection. After analyzing data, some colleagues advised us to conduct IGRA for TST confirmation. According to such doubtful results, using TST for LTBI screening needs further cost-effectiveness analysis.

Limitations of the study

For some patients, the researcher had to visit several times to contact the patient. No definite officially recorded history of BCG vaccination was present.

Authors' contribution

Conceptualization: AA, AZM.

Methodology: PN.
Validation: PN, BH, AA.
Formal analysis: PN, BH, AA.
Investigation: AZM, BH.
Resources: AZM, PN.
Data Curation: BH, AA.
Visualization: PN, AA, AZM.
Supervision: PN, AA, AZM.
Project administration: AA.
Writing–original draft: AZM, AA, BH.
Writing–review and editing: PN, AA, AZM.

Conflicts of interest

The authors declare that they have no conflict of interest.

Ethical issues

This study followed the ethical standards of the Helsinki Declaration. The ethics committee of Lorestan University of Medical Sciences approved this study (IR.LUMS.REC.1397.078). Written informed consent was obtained from all participants before any intervention. This study was extracted from the M.D thesis of Pardis Nasiri at that university (Thesis #899). Additionally, ethical issues including plagiarism, data fabrication, double publication have been completely observed by the authors.

Funding/Support

The research was funded by the Deputy of Research and Technology of Lorestan University of Medical Sciences (Grant #842).

References

1. WHO. Tuberculosis. 2021[cited 2021 Oct 27]. Available from: https://www.who.int/news-room/fact-sheets/detail/tuberculosis.
2. Glaziou P, Floyd K, Raviglione M. Global burden and epidemiology of tuberculosis. Clin Chest Med. 2009;30:621-36. doi: 10.1016/j.ccm.2009.08.017.
3. WHO. Latent Tuberculosis Infection. 2015 [cited 2021 June 11]. Available from: https://www.who.int/tb/challenges/ltbi_factsheet_2014.pdf.
4. Sester M, Sester U, Clauer P, Heine G, Mack U, Moll T, et al. Tuberculin skin testing underestimates a high prevalence of latent tuberculosis infection in hemodialysis patients. Kidney Int. 2004;65:1826-34. doi: 10.1111/j.1523-1755.2004.00586.x.
5. Romanowski K, Clark EG, Levin A, Cook VJ, Johnston JC. Tuberculosis and chronic kidney disease: an emerging global syndemic. Kidney Int. 2016;90:34-40. doi: 10.1016/j.kint.2016.01.034.
6. Smirnoff M, Patt C, Seckler B, Adler JJ. Tuberculin and anergy skin testing of patients receiving long-term hemodialysis. Chest. 1998;113:25-7. doi: 10.1378/chest.113.1.25.
7. Kamal IMA, Mahdi BM. Seroprevalence occurrence of viral hepatitis and HIV among hemodialysis patients. Ann Med Surg (Lond). 2018;29:1-4. doi: 10.1016/j.amsu.2018.03.018.
8. Cohen G, Hörl WH. Immune dysfunction in uremia—an update. Toxins (Basel). 2012;4:962-90. doi: 10.3390/toxins4110962.
9. Meijers RW, Litjens NH, de Wit EA, Langerak AW, van der Spek A, Baan CC, et al. Uremia causes premature ageing of the T cell compartment in end-stage renal disease patients. Immun Ageing. 2012;9:19. doi: 10.1186/1742-4933-9-19.
10. Segall L, Covic A. Diagnosis of Tuberculosis in Dialysis Patients: Current Strategy. Clin J Am Soc Nephrol. 2010;5:1114–1122. doi: 10.2215/CJN.09231209.
11. Rao TM, Ram R, Swarnalatha G, Santhosh Pai BH, Ramesh V, Rao CS, et al. Tuberculosis in haemodialysis patients: A single centre experience. Indian J Nephrol. 2013;23:340-5. doi: 10.4103/0971-4065.116296.
12. El Kabbaj D, Bahadi A, Oualim Z. Prevalence of tuberculosis in hemodialysis patients. Saudi J Kidney Dis Transpl. 2010;21:164-7.
13. WHO. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management; 2018 [cited 2021 Jun 2]. Available from: https://www.who.int/publications/i/item/9789241550239.
14. CD. Testing in BCG-Vaccinated Persons; c2016 (cited 2021 June) Available from: https://www.cdc.gov/tb/topic/testing/testingbcgvaccinated.htm.
15. WHO. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. 2018 [cited 2021 Jun 2]. Available from: https://www.who.int/publications/i/item/9789241550239.
16. United States Renal Data System. 2020 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2020. Available from: https://adr.usrds.org/2020.
17. Shu CC, Hsu CL, Wei YF, Lee CY, Liou HH, Wu VC, et al . Risk of Tuberculosis Among Patients on Dialysis: The Predictive Value of Serial Interferon-Gamma Release Assay. Medicine (Baltimore). 2016;95:e3813. doi: 10.1097/MD.0000000000003813.
18. Anibarro L, Trigo M, Feijoó D, Ríos M, Palomares L, Pena A, et al. Value of the tuberculin skin testing and of an interferon-gamma release assay in haemodialysis patients after exposure to M. tuberculosis. BMC Infect Dis. 2012;12:195. doi: 10.1186/1471-2334-12-195.
19. Lee SS, Chou KJ, Dou HY, Huang TS, Ni YY, Fang HC, et al. High prevalence of latent tuberculosis 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.01790210.
20. Hussein MT, Yousef LM, Ali AT. Detection of latent tuberculosis infection in hemodialysis patients: Comparison between the quantiferon-tuberculosis gold test and the tuberculin skin test. Egypt J Bronchol. 2017;11:255-9. doi: 10.4103/ejb.ejb_19_17.
21. Madegedara D, Perera B, Senevirathna S. Prevalence of latent tuberculosis in patients with chronic kidney disease of non diabetic origin in Central Sri Lanka. European Respiratory Journal. 2020;56:1672. doi: 10.1183/13993003.congress-2020.1672
22. Shu CC, Hsu CL, Lee CY, Wang JY, Wu VC, Yang FJ, et al. Comparison of the prevalence of latent tuberculosis

infection among non-dialysis patients with severe chronic kidney disease, patients receiving dialysis, and the dialysis-unit staff: a cross-sectional study. PLoS One. 2015;10:e0124104. doi: 10.1371/journal.pone.0124104.
23. Wu CH, Su HA, Chou CA, Liu JW, Lee CT, Dai LH, et al. An observational study on prevalence of latent tuberculosis infection and outcome of 3HP treatment in patients under hemodialysis in Taiwan. J Formos Med Assoc. 2021;120:1350-60. doi: 10.1016/j.jfma.2020.10.008.
24. Starke JR. Tuberculosis skin testing: New schools of thought. J Am Acad Pediatr. 1996;98:123–5.
25. Wang L, Turner MO, Elwood RK, Schulzer M, FitzGerald JM. A meta-analysis of the effect of Bacille Calmette Guérin vaccination on tuberculin skin test measurements. Thorax. 2002;57:804-9. doi: 10.1136/thorax.57.9.804.
26. Rogerson TE, Chen S, Kok J. Tests for latent tuberculosis in people with ESRD: a systematic review. Am J Kidney Dis. 2013;61:33-43. doi: 10.1053/j.ajkd.2012.07.019.
27. Ferguson TW, Tangri N, Macdonald K, Hiebert B, Rigatto C, Sood MM, et al. The diagnostic accuracy of tests for latent tuberculosis infection in hemodialysis patients: a systematic review and meta-analysis. Transplantation. 2015;99:1084-91. doi: 10.1097/TP.0000000000000451.
28. Zwerling A, Behr MA, Verma A, Brewer TF, Menzies D, Pai M. The BCG World Atlas: a database of global BCG vaccination policies and practices. PLoS Med. 2011;8:e1001012. doi: 10.1371/journal.pmed.1001012.
29. CDC. Tuberculin Skin Testing. 2020 [cited 2021 Sep]. Available from: https://www.cdc.gov/tb/publications/factsheets/testing/skintesting.pdf.
30. Lewinsohn DM, Leonard MK, LoBue PA, Cohn DL, Daley CL, Desmond E, et al. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin Infect Dis. 2017;64:111-5. doi: 10.1093/cid/ciw778.
31. Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? Int J Tuberc Lung Dis. 2006;10:1192-204.
32. Pai M, Zwerling A, Menzies D. Systematic review: T-cell-based assays for the diagnosis of latent tuberculosis infection: an update. Ann Intern Med. 2008;149:177-84. doi: 10.7326/0003-4819-149-3-200808050-00241.
33. Diel R, Goletti D, Ferrara G, Bothamley G, Cirillo D, Kampmann B, et al. Interferon-γ release assays for the diagnosis of latent Mycobacterium tuberculosis infection: a systematic review and meta-analysis. Eur Respir J. 2011;37:88-99. doi: 10.1183/09031936.00115110.
34. Mancuso JD, Mody RM, Olsen CH, Harrison LH, Santosham M, Aronson NE. The long-term effect of Bacille Calmette-Guérin vaccination on tuberculin skin testing: a 55-year follow-up study. Chest. 2017;152:282-94. doi: 10.1016/j.chest.2017.01.001.
35. Diel R. Long-term effect of Bacille Calmette-Guérin vaccination in tuberculin skin testing: a new reality for TB prevention. Chest. 2017;152:235-236. doi: 10.1016/j.chest.2017.03.011.
36. Gudjónsdóttir MJ, Kötz K, Nielsen RS, Wilmar P, Olausson S, Wallmyr D, et al. Relation between BCG vaccine scar and an interferon-gamma release assay in immigrant children with "positive" tuberculin skin test (≥10 mm). BMC Infect Dis. 2016;16:540. doi: 10.1186/s12879-016-1872-9.
37. Kumar CM, Bedi N. Tuberculin Conversion after BCG Vaccination. Indian Pediatr. 2019;56:141-142.
38. Montane Jaime LK, Akpaka PE, Vuma S, Justiz-Vaillant AA. A healthy patient with positive mantoux test but negative quantiferon Gold assay and no evidence of risk factors - to treat or not to treat? IDCases. 2019;18:e00658. doi: 10.1016/j.idcr.2019.e00658.
39. Seddon JA, Paton J, Nademi Z. The impact of BCG vaccination on tuberculin skin test responses in children is age dependent: evidence to be considered when screening children for tuberculosis infection. Thorax. 2016;71:932-9. doi: 10.1136/thoraxjnl-2015-207687.