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ORIGINAL ARTICLE

Risk of tuberculosis in children with rheumatologic diseases treated with biological agents: A cross-sectional cohort study

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ABSTRACT

Objectives: This study aimed to evaluate the risk of tuberculosis (TB) disease in children receiving biological agents for rheumatologic diseases, focusing on appropriate screening tests in a high-priority country for TB control.

Patients and methods: One hundred nine children (56 females, 53 males; range, 3.4 to 16.2 years) who received any biological agent for rheumatologic diseases for more than two years between May 2012 and October 2021 were included in this retrospective study. Patients were screened for TB infection using tuberculin skin test (TST) or interferon-gamma release assay (IGRA). Following the initial evaluation, patients were clinically examined for TB every three months by a comprehensive medical history and physical examination, and every 12 months using TST or IGRA.

Results: At the initiation of the biological agent, the patients' mean age was 12.4±4.5 years. The average follow-up duration was 3.6±1.3 years (range, 2.6 to 10.2 years) for patients treated with biological agents. Each patient had a documented Bacillus Calmette-Guérin vaccination. Before the initiating of therapy, TST was performed alone in 45 (41.3%) patients and in combination with IGRA in 64 (58.7%) patients. In the 64 patients who underwent both TST and IGRA, IGRA revealed nine (14.1%) positive results. Six (66.7%) of these nine patients, however, had negative baseline TST. Four (7.3%) of the 55 individuals whose initial IGRA results were negative also had positive TST results. Overall, no TB disease was observed after a follow-up period.

Conclusion: This study reveals that biological agents were not associated with an increased risk of TB disease in closely monitored children. Additionally, the concomitant use of TST and IGRA for screening of TB is reasonable in patients receiving biological agents.

Keywords: Biological agents, children, interferon-gamma release assay, screening, tuberculin skin test.

Within the last two decades, biological agents that block the effects of tumor necrosis factor, such as infliximab, adalimumab, and etanercept, as well as interleukin-targeted agents, such as anakinra, tocilizumab, canakinumab, have been approved for the treatment of rheumatologic diseases.[1] Despite their well-established therapeutic benefits, they are associated with an increased risk of developing active tuberculosis (TB) disease as a result of latent TB infection (LTBI) reactivation.[2-5]

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Screening of LTBI is recommended for patients prior to administration and during the course of biological agents. Although there is no gold standard test for LTBI diagnosis, tuberculin skin test (TST) and interferon-gamma release assay (IGRA) are commonly used for screening.[6] The test strategies may differ depending on the recommendations of countries, the endemicity of TB, and the immune status of the patients.[7] To date, a limited number of studies have focused on pediatric populations. Little data on children is available as the majority of studies are focused on adult populations.[8-14] Furthermore, the majority of studies included patients from regions with low TB prevalence or evaluated individuals who had not been vaccinated with Bacillus Calmette-Guérin (BCG), which should be considered when interpreting the data.

Despite a decline in TB incidence to 14.6 per 100,000 in 2017, Türkiye is still one of the high-priority countries for TB control.[15,16] According to Turkish Ministry of Health guidelines, TST is the recommended method for LTBI screening, with IGRA being used only in exceptional circumstances, such as immunosuppression and TST negativity in individuals with clinically high suspicion of TB disease.[15] As a result of conflicting data regarding the optimal screening test strategies for LTBI prior to administration and during treatment with biological agents for rheumatologic diseases in children, this study aimed to evaluate the risk of TB disease in patients with various rheumatologic diseases receiving biological agents, with a particular emphasis on appropriate screening strategies for LTBI and the performance of TST and IGRA in children in a country where BCG vaccination is still mandatory.

PATIENTS AND METHODS

This retrospective study included 109 children (56 females, 53 males; range, 3.4 to 16.2 years years) treated with biological agents for a variety of rheumatologic diseases in Dr. Behçet Uz Children's Hospital, which is a pediatric referral and tertiary care hospital in Izmir. Children who received any biological agent as monotherapy for more than two years and followed by both outpatient clinics of the pediatric rheumatology and pediatric infectious diseases between May 2012 and October 2021 were included in the study. Data on the patients' demographic characteristics (age, sex, and medical history), underlying rheumatologic diseases, comorbidities, initiation and duration of antirheumatic therapy, treatment outcome, history of TB contact, presence of BCG scar, and screening results for TB infection or disease were collected from medical records. Patients with a history of active or latent TB, as well as those with less than a two-year follow-up period after receiving the biological agents, were excluded from the study. All patients enrolled in the study were examined by the division of pediatric infectious diseases for signs and symptoms of active TB prior to and during antirheumatic therapy in accordance with the valid and current Turkish Ministry of Health guidelines for the use of biological agents.[15,17]

Screening for tuberculosis

Each patient was evaluated for signs of active or previous TB infection and underwent a standard TST or an IGRA (QuantiFERON-TB Gold Plus® test; Cellestis, Carnegie, Australia) and a chest radiograph prior to the administration of the biological agent. Due to the availability of the IGRA at the study center, all patients were screened for LTBI with only TST before April 2019 and both TST and IGRA after and during April 2019. Following the initial evaluation, patients were clinically reevaluated for a TB infection every three months with a detailed medical history and physical examination, every six months with a chest radiograph, and every year with TST or IGRA.

Tuberculin skin test

A standard TST was performed by the Mantoux method of 0.1 mL (5 IU) of PPD according to current recommendations.[18] A trained physician measured the diameter of cutaneous induration 72 h later. At the time of initial evaluation prior to therapy, the test was considered positive for immunocompetent patients when the transverse diameter of induration was ≥15 mm for BCG-vaccinated patients and ≥10 mm for BCG-unvaccinated patients. An induration of ≥5 mm was considered positive in immunocompromised patients who are candidates for the use of biological agents for rheumatologic diseases.[15,17]

Interferon-gamma release assay

Interferon-gamma release assay was performed in accordance with the manufacturer's recommendations.[19] Blood samples were analyzed in four distinct tubes; nil tube, TB antigen tube 1, TB antigen tube 2, and mitogen tube as a positive control. Both TB antigen tubes contained peptide antigens derived from the *Mycobacterium tuberculosis* complex-associated antigens, ESAT-6 (early secreted antigenic target 6), and CFP-10 (culture filtrate protein 10). The tubes were incubated at 37°C for 16 to 24 h. The plasma was removed by centrifugation, and the amount of interferon-gamma (IFN-γ; IU/mL) was measured by enzyme-linked immunosorbent assay. Interferon-gamma release assay was considered positive for an IFN-γ response to either TB antigen tube that was significantly above the nil IFN-γ (IU/mL) value. Tests were interpreted as indeterminate if the mitogen minus nil was <0.5 or the nil was >8.0; tests were interpreted as negative if the TB antigen minus nil was <0.35 or if the TB antigen minus nil was ≥0.35 but was <25% of the nil value; tests were interpreted as positive if the TB antigen minus nil was ≥0.35 and was ≥25% of the nil value.[19] If active TB was ruled out, patients with a positive TST or IGRA result were diagnosed with LTBI and oral isoniazid prophylaxis at a dose of 10 mg/kg was started one month prior to the first dose of biological agent and continued for nine months.

Statistical analysis

Data were analyzed using IBM SPSS version 20.0 (IBM Corp., Armonk, NY, USA). Categorical variables were analyzed using a chi-square test or Fisher exact test. Cohen's kappa coefficient was calculated to further evaluate the agreement between the TST and the IGRA assay. A p value <0.05 was considered statistically significant.

RESULTS

The study included 109 pediatric patients with various rheumatic diseases, including 74 (67.9%) with juvenile idiopathic arthritis, 29 (26.6%) with familial Mediterranean fever, three (2.8%) with periodic fever syndromes, and one patient each with spondyloarthropathy, uveitis, and Behçet's disease. The mean age of patients at the time of biological agent initiation was 12.4±4.5 years. Canakinumab was the most frequently prescribed drug (n=37, 33.9%) during the study period, followed by adalimumab (n=35, 32.1%), etanercept (n=25, 22.9%), and tocilizumab (n=12, 11.1%). The average follow-up period was 3.6±1.3 years (range, 2.6 to 10.2 years). Clinical and demographic characteristics of the study population are shown in Table 1.

All patients had a documented BCG vaccination through the presence of a scar, and none had any prior exposure to known TB contacts. TST alone was utilized in 45 (41.3%) patients for TB screening prior to initiating a biological agent, and a combination of TST and IGRA was used in 64 (58.7%) patients. The screening test results are summarized in Table 2.

Positive results were detected in six cases (6/45, 13.3%) who had only TST performed. Among 64 patients who underwent a combination of TST and IGRA, IGRA revealed nine (14.1%) positive results. However, six (66.7%) of these nine patients had a negative TST at the baseline. Four (7.3%) of the 55 patients who were initially negative for IGRA were positive for TST. Data are shown in Figure 1.

The reliability between TST and IGRA was estimated by Cohen's kappa coefficient, and

Table 1. Clinical and demographic characteristics of the study population (n=109)

	n	%	Mean±SD
Age (year)			12.4±4.5
Sex			
Female	56	51.4	
Follow-up period (year)			3.6±1.3
Underlying diseases			
Juvenile idiopathic arthritis	74	67.9	
Familial Mediterranean fever	29	26.6	
Periodic fever syndromes	3	2.8	
Uveitis	1	0.9	
Spondyloarthropathy	1	0.9	
Behçet's disease	1	0.9	
Biological agents			
Adalimumab	35	32.1	
Etanercept	25	22.9	
Canakinumab	37	33.9	
Tocilizumab	12	11.1	

SD: Standard deviation.

Table 2. Screening test results of patients for latent tuberculosis infection prior to initiating biologic agents

	TST (-)	TST (+)	IGRA (-)	IGRA (+)	IGRA (+) TST (+)	IGRA (+) TST (-)	IGRA (-) TST (+)	IGRA (-) TST (-)
Number of patients screened with TST alone (n=45)	39	6	NA	NA	NA	NA	NA	NA
Number of patients screened with both TST and IGRA (n=64)	59	5	55	9	3	6	4	51
Total	98	11	55	9	3	6	4	51

TST: Tuberculin skin test; IGRA: Interferon-gamma release assay; NA: Not applicable; + Positive for test result; – Negative for test result.

there was a strong agreement between these tests (κ=0.833; 95% confidence interval: 0.738-0.927; p<0.001).

As a result of positivity for TST or IGRA, isoniazid monotherapy for LTBI was applied in 27 patients for a period of nine months. During follow-up, 10 patients had TST seroconversion. Seroconversion was observed in seven patients who received canakinumab, two patients who received adalimumab, and one patient who received etanercept. During the study period, no TB disease was observed.

DISCUSSION

In this study, 109 patients with rheumatologic diseases who were treated with biological agents were evaluated for LTBI and TB disease using TST or IGRA. Close monitoring for LTBI is required owing to the increased likelihood of TB during the treatment of pediatric rheumatologic diseases. The current study demonstrates that none of the children receiving biological agents was diagnosed as TB after a mean follow-up of 3.6±1.3 years in an area with a high-priority for TB control[16] and in a region with a high level of immigration from countries with a high TB burden. It was detected that 66.7% of the patients who were positive for IGRA before treatment had negative baseline TST. Furthermore, four (7.3%) of the initially IGRA-negative patients were positive for TST. As a result, it would be appropriate to use the two tests together since screening with only one test may fail to distinguish LTBI in immunocompromised patients.

Although the use of biological agents may increase the risk of progression to active TB, none of the 109 patients in the current study had been diagnosed with active TB disease. Likewise, limited studies in children, even in areas with an intermediate incidence of TB, indicated that biological agents did not

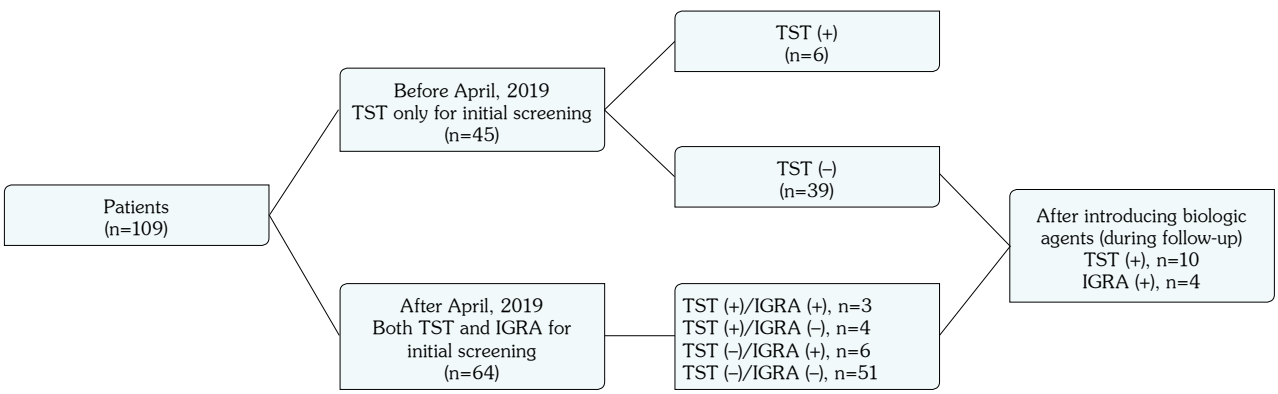

Figure 1. Flow chart of screening test results for tuberculosis infection.
TST: Tuberculin skin test; IGRA: Interferon-gamma release assay.

significantly increase the risk of TB in children with juvenile idiopathic arthritis.[20,21] However, the majority of studies derive their results on a shorter period of follow-up.[22] All patients in the current study were followed for an average of more than three years. While this prolonged assessment period may be appropriate for identifying the effect of agents on the risk of TB disease, there are no adequate studies evaluating the longer periods of follow-up for children through adulthood. As a result, it is reasonable to speculate that biological agents do not contribute to the development of TB disease in children.

Screening patients for LTBI and initiating chemoprophylaxis if positive is critical for reducing TB reactivation. Although the recommendations vary depending on the economic status and TB prevalence of a country, the TST, IGRA, or both, in combination with chest radiographs, are the approved LTBI screening procedures.[21,23,24] While the World Health Organization recommends TST or IGRA for LTBI screening, there is no gold standard for the LTBI diagnosis.[19]

There are no well-designed randomized controlled trials in children examining the priority of TST or IGRA. Furthermore, these studies were frequently carried out in areas with low TB prevalence and with individuals who were not vaccinated with BCG. On the other hand, TSTs tend to yield a high rate of false-positive results in regions where TB is endemic or where BCG immunization is common.[25] Several studies have also reported false-negative TST results in patients receiving immunosuppressive therapy for rheumatologic diseases.[26-28] However, IGRAs may have some advantages, particularly in the case of people who are vaccinated with BCG.[29] In the current study, both two tests showed considerable agreement, as confirmed by Cohen's kappa coefficient, which was 0.833. Considering the possibility of false-negative test results, the concomitant use of TST and IGRA may provide more reliable information in the diagnosis of LTBI.[30,31] This study revealed that screening patients with TST alone prior to biological agent treatment might miss six (9.4%) cases of LTBI; additionally, two of these six patients developed TST seroconversion during the treatment. Four (6.3%) patients with TST positivity were negative for IGRA but were later found to be positive for IGRA during follow-up. In these circumstances, concomitant use of TST and IGRA for screening patients prior to biological agent administration is reasonable. In other words, 15.6% of patients would have been treatment-naive in a high-priority country for TB control, where preventive therapy is critical to lowering the risk of progression to active disease, especially in children with altered immune status or who have been exposed to any biological agent.

Several limitations should be considered while interpreting the results. First, this was a retrospective study, which has inherent limitations compared to randomized clinical trials. Second, patients who were administered various biologic agents were evaluated. Therefore, the patients may not have a similar risk of developing TB. Third, the patients were not followed through adulthood; the course of TB disease is more prominent in adults than in children. However, it should be emphasized that the current study includes one of the largest pediatric populations with rheumatologic diseases who were screened for LTBI prior to initiating biological agents and followed for a reasonable period during the treatment to determine the risk of developing active TB. Moreover, this study was conducted in a high-priority country for TB control and in an area with a high rate of immigration from countries with a high TB burden.

In conclusion, despite reports that there is a relationship between the use of biological agents and the development of TB, the present study demonstrates that biological agents are not associated with an increased risk of TB disease in closely followed children with various rheumatologic diseases. It is critical to screen children for LTBI before and during treatment and to administer chemoprophylaxis if positive to reduce TB reactivation. Therefore, concomitant use of TST and IGRA is a more reliable screening strategy for children in countries with higher TB prevalence.

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Ethics Committee (date: 17.12.2020, no: 2020/17-09). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from the parents of the patients.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Conceptualization and methodology: N.B., İ.D.; Data collection: E.K., E.B., Ş.Ş., A.A.K., K.Ö.A., B.M., Ö.A.G.; Writing: N.B., E.B., Y.S., İ.D.; Editing: N.B., E.K., Ö.A.G., B.M.; All authors read and approved the final manuscript.

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REFERENCES

1. Horneff G. Biologic-associated infections in pediatric rheumatology. Curr Rheumatol Rep 2015;17:66. doi: 10.1007/s11926-015-0542-z.
2. Lalvani A, Millington KA. Screening for tuberculosis infection prior to initiation of anti-TNF therapy. Autoimmun Rev 2008;8:147-52. doi: 10.1016/j.autrev.2008.07.011.
3. Gabriele F, Trachana M, Simitsopoulou M, Pratsidou-Gertsi P, Iosifidis E, Pana ZD, et al. Performance of QuantiFERON®-TB Gold In-Tube assay in children receiving disease modifying anti-rheumatic drugs. World J Pediatr 2017;13:472-8. doi: 10.1007/s12519-017-0050-5.
4. Vortia E, Uko VE, Yen-Lieberman B, Frawley J, Worley SE, Danziger-Isakov L, et al. Low indeterminate rates associated with use of the QuantiFERON-TB Gold In-Tube test in children with inflammatory bowel disease on long-term infliximab. Inflamm Bowel Dis 2018;24:877-82. doi: 10.1093/ibd/izx077.
5. Brassard P, Lowe AM, Bernatsky S, Kezouh A, Suissa S. Rheumatoid arthritis, its treatments, and the risk of tuberculosis in Quebec, Canada. Arthritis Rheum 2009;61:300-4. doi: 10.1002/art.24476.
6. Haas MK, Belknap RW. Diagnostic tests for latent tuberculosis infection. Clin Chest Med 2019;40:829-37. doi: 10.1016/j.ccm.2019.07.007.
7. Kavadichanda C, Adarsh MB, Ajmani S, Maccora I, Balan S, Ramanan AV, et al. Tuberculosis in children with rheumatic diseases treated with biologic disease-modifying anti-rheumatic drugs. Mediterr J Rheumatol 2021;32:290-315. doi: 10.31138/mjr.32.4.290.
8. Dumaine C, Bekkar S, Belot A, Cabrera N, Malik S, von Scheven A, et al. Infectious adverse events in children with juvenile idiopathic arthritis treated with biological agents in a real-life setting: Data from the JIRcohorte. Joint Bone Spine 2020;87:49-55. doi: 10.1016/j.jbspin.2019.07.011.
9. Quartier P, Allantaz F, Cimaz R, Pillet P, Messiaen C, Bardin C, et al. A multicentre, randomised, double-blind, placebo-controlled trial with the interleukin-1 receptor antagonist anakinra in patients with systemic-onset juvenile idiopathic arthritis (ANAJIS trial). Ann Rheum Dis 2011;70:747-54. doi: 10.1136/ard.2010.134254.
10. Lovell DJ, Giannini EH, Reiff A, Cawkwell GD, Silverman ED, Nocton JJ, et al. Etanercept in children with polyarticular juvenile rheumatoid arthritis. Pediatric Rheumatology Collaborative Study Group. N Engl J Med 2000;342:763-9. doi: 10.1056/NEJM200003163421103.
11. Ruperto N, Lovell DJ, Cuttica R, Wilkinson N, Woo P, Espada G, et al. A randomized, placebo-controlled trial of infliximab plus methotrexate for the treatment of polyarticular-course juvenile rheumatoid arthritis. Arthritis Rheum 2007;56:3096-106. doi: 10.1002/art.22838.
12. Stoll ML, Gotte AC. Biological therapies for the treatment of juvenile idiopathic arthritis: Lessons from the adult and pediatric experiences. Biologics 2008;2:229-52. doi: 10.2147/btt.s2210.
13. Ruperto N, Lovell DJ, Quartier P, Paz E, Rubio-Pérez N, Silva CA, et al. Long-term safety and efficacy of abatacept in children with juvenile idiopathic arthritis. Arthritis Rheum 2010;62:1792-802. doi: 10.1002/art.27431.
14. Horneff G, Burgos-Vargas R, Constantin T, Foeldvari I, Vojinovic J, Chasnyk VG, et al. Efficacy and safety of open-label etanercept on extended oligoarticular juvenile idiopathic arthritis, enthesitis-related arthritis and psoriatic arthritis: Part 1 (week 12) of the CLIPPER study. Ann Rheum Dis 2014;73:1114-22. doi: 10.1136/annrheumdis-2012-203046.
15. Diagnosis and Treatment Guideline for Tuberculosis, Turkish Ministry of Health, Ankara, 2019. Available at: https://hsgm.saglik.gov.tr/depo/birimler/tuberkuloz_db/haberler/Tuberkuloz_Tani_Ve_Tedavi_Rehberi_/Tuberkuloz_Tani_ve_Tedavi_Rehberi_08.07.2019_Yuksek_KB.pdf.
16. Tuberculosis. World Health Organization. Available at: http://www.euro.who.int/en/health-topics/communicable-diseases/tuberculosis/tuberculosis-read-more.
17. Diagnosis and Treatment Guideline for Tuberculosis, Turkish Ministry of Health, Ankara, 2011. Available at: https://toraks.org.tr/site/sf/documents/pre_migration/0843354699a1757b76dde91155e96a9f72d0604ec89c5ed967e4db07dc77ad02.pdf. [Accessed: 20.02.2021].
18. Girlanda S, Mantegani P, Baldissera E, Aiello P, Ratti M, Sabbadini MG, et al. ELISPOT-IFN-gamma assay instead of tuberculin skin test for detecting latent Mycobacterium tuberculosis infection in rheumatic patients candidate to anti-TNF-alpha treatment. Clin Rheumatol 2010;29:1135-41. doi: 10.1007/s10067-010-1532-1.

19. QuantiFERON-TB Gold Plus (QFT-Plus) ELISA Package Insert 03/2018. Catalog number: 622120, 622822.
20. Hsin YC, Zhuang LZ, Yeh KW, Chang CW, Horng JT, Huang JL. Risk of tuberculosis in children with juvenile idiopathic arthritis: A nationwide population-based study in Taiwan. PLoS One 2015;10:e0128768. doi: 10.1371/journal.pone.0128768.
21. Kilinc AA, Onal P, Oztosun B, Yildiz M, Adrovic A, Sahin S, et al. Determination of tuberculin skin test for isoniazid prophylaxis in BCG vaccinated children who are using anti-TNF agents for rheumatologic diseases. Pediatr Pulmonol 2020;55:2689-96. doi: 10.1002/ppul.24963.
22. Aygun D, Sahin S, Adrovic A, Barut K, Cokugras H, Camcıoglu Y, et al. The frequency of infections in patients with juvenile idiopathic arthritis on biologic agents: 1-year prospective study. Clin Rheumatol 2019;38:1025-30. doi: 10.1007/s10067-018-4367-9.
23. Goletti D, Petrone L, Ippolito G, Niccoli L, Nannini C, Cantini F. Preventive therapy for tuberculosis in rheumatological patients undergoing therapy with biological drugs. Expert Rev Anti Infect Ther 2018;16:501-12. doi: 10.1080/14787210.2018.1483238.
24. Aygün D, Yıldırım T, Öner ÖB, Şiraneci R. Evaluation of clinical and laboratory characteristics of childhood tuberculosis. Turk Pediatri Ars 2020;55:236-43. doi: 10.14744/TurkPediatriArs.2020.02438.
25. Xie X, Chen JW, Li F, Tian J, Gao JS, Zhang D. A T-cell-based enzyme-linked immunospot assay for tuberculosis screening in Chinese patients with rheumatic diseases receiving infliximab therapy. Clin Exp Med 2011;11:155-61. doi: 10.1007/s10238-010-0123-4.
26. Ponce de León D, Acevedo-Vásquez E, Sánchez-Torres A, Cucho M, Alfaro J, Perich R, et al. Attenuated response to purified protein derivative in patients with rheumatoid arthritis: Study in a population with a high prevalence of tuberculosis. Ann Rheum Dis 2005;64:1360-1. doi: 10.1136/ard.2004.029041.
27. Pai M, Denkinger CM, Kik SV, Rangaka MX, Zwerling A, Oxlade O, et al. Gamma interferon release assays for detection of Mycobacterium tuberculosis infection. Clin Microbiol Rev 2014;27:3-20. doi: 10.1128/CMR.00034-13.
28. Richeldi L, Losi M, D'Amico R, Luppi M, Ferrari A, Mussini C, et al. Performance of tests for latent tuberculosis in different groups of immunocompromised patients. Chest 2009;136:198-204. doi: 10.1378/chest.08-2575.
29. Jeong DH, Kang J, Jung YJ, Yoo B, Lee CK, Kim YG, et al. Comparison of latent tuberculosis infection screening strategies before tumor necrosis factor inhibitor treatment in inflammatory arthritis: IGRA-alone versus combination of TST and IGRA. PLoS One 2018;13:e0198756. doi: 10.1371/journal.pone.0198756.
30. Marino A, Chiappini E, Cimaz R, Simonini G. Prebiologic therapy tuberculosis screening experience in a pediatric rheumatology center: TST and IGRA are both necessary. Pediatr Infect Dis J 2017;36:440-1. doi: 10.1097/INF.0000000000001466.
31. Gomes CMF, Terreri MT, Moraes-Pinto MI, Pinheiro MM. Performance of 4 methods for screening of latent tuberculosis infection in patients with chronic inflammatory arthritis under TNFα inhibitors: A 24-month prospective study. Adv Rheumatol 2021;61:71. doi: 10.1186/s42358-021-00226-z.