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Re: Interferon-gamma Release Assay Agreement With Tuberculin Skin Test in Pretransplant Screening for Latent Tuberculosis in a High-prevalence Country

Dear Editor,

We read with interest the article published by Savaj and colleagues in the past issue of the *Iranian Journal of Kidney Diseases*.¹ Tuberculosis (TB) is a serious public health problem. It is the second most frequent cause of death of infectious diseases worldwide with about 2 million deaths per year,² and one of the most important infectious diseases in Iran. The incidence of active tuberculosis among patients on long-term dialysis is 6.9 to 52.5 times higher than in the general population.^{3,4} In hemodialysis patients, there is a relative compromise in acquired cell-mediated immunity, which constitutes the major determinant of host resistance for further development of disease.⁵ Tuberculosis is a serious infection affecting organ transplant recipients including kidney transplant recipients. Development of TB occurs in transplant recipients 20 to 74 times more than it does in the general population. The diagnosis and management of TB in this group is challenging, because the presenting symptoms can be atypical, and the therapy may lead to potential toxicity or interactions with immunosuppressive medications.⁶

Because of the increased prevalence of latent TB infection in dialysis patients and the high risk of developing active disease, screening for latent

TB infection in this population prior to kidney transplantation is recommended. The tuberculin skin test (TST), which is the classic diagnostic tool for latent TB infection has several major drawbacks, including poor sensitivity (high prevalence of anergy) and specificity (false positive tests in those vaccinated).⁷ In recent years, new immunological assays that measure lymphocyte response to stimulation of ESAT-6 and CFP-10 antigens from *Mycobacterium tuberculosis*, called interferon- γ release assays (IGRAs), including QuantiFERON Gold IT and T-spot TB, have become available and appear to be more reliable in immunosuppressed populations. These assays are not affected by previous vaccination, thus with superior sensitivity and specificity compared to the previously available tests for the diagnosis of TB.⁷

Savaj and colleagues reported the results of screening of latent TB infection in hemodialysis patients who were candidates for kidney transplantation. Tuberculin skin test and IGRA were positive in 43.5% and 23.4%, respectively with poor correlation. The authors, however, have not explained the reason of the discordant results.¹ When compared to TST, IGRAs have some operational advantages that are particularly relevant in immunocompromised patients. QuantiFERON

Gold IT has positive and negative control which allows discrimination between anergy and true negative,⁸ which has not been mentioned in this article. At present, the advantage of either test for posttransplant risk-assessment is not known. Tuberculin skin test and IGRA have poor correlation in detecting latent TB infection among transplant candidate. As a result, the best screening tests for detecting latent TB infection in transplant candidates is unclear, as the positive predictive value for the development of TB in this setting is largely unknown and varies with TB prevalence.^{6,8} Given the discordant results between IGRAs and TST in several studies in transplant candidates, a combination of both assays may result in a higher sensitivity if false negativity is a concern.^{6,8,9}

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