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REVIEW ARTICLE

Mycobacterium tuberculosis Infection in Liver Transplantation

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Mycobacterium tuberculosis can cause significant infections in liver transplant candidates and recipients. Its nonspecific clinical features and prolonged growth time in culture make the diagnosis difficult, and treating tuberculosis (TB) remains challenging because of significant toxicities and drug-drug interactions. The diagnosis of a latent TB infection may be accomplished with tuberculin skin testing and with the newer interferon-γ release assays, although this infection may be underrecognized because of host factors. Latent TB should be treated, but the degree of liver failure and the likelihood of progression to active TB will dictate whether this should occur before or after transplantation. Patients who have a history of TB, have used muromonab-CD3 or anti-T lymphocyte antibodies, or have experienced allograft rejection or coinfection with cytomegalovirus, *Pneumocystis jiroveci*, or *Nocardia* are at the greatest risk of developing active TB. Active TB in transplant patients is difficult to treat because of drug-induced hepatotoxicity and the significant interaction between rifampin and calcineurin inhibitors. In this article, we review the epidemiology, clinical features, and evaluation of transplant candidates and recipients. In addition, we offer recommendations on the appropriate diagnostic and treatment regimens for patients with latent and active TB infections. ***Liver Transpl 16:1129-1135, 2010.*** © **2010 AASLD.**

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Tuberculosis (TB) is a serious global infection with an estimated prevalence of 13.7 million cases worldwide.[1] Transplant recipients have a 36- to 74-fold higher risk of developing TB versus the general population.[2] TB in liver transplant recipients presents unique challenges, including a delayed diagnosis secondary to insensitive testing and treatment complications due to antituberculous drug toxicities and interactions with immunosuppressive agents. This review focuses on the epidemiology, clinical features, diagnosis, clinical evaluation, and treatment of liver transplant patients infected with TB.

EPIDEMIOLOGY

Rates of 0.47% to 2.3% for active TB in adult liver transplant recipients has been reported.[2–5] Because of the difficulty of accurately diagnosing symptomatic TB, these figures most likely underestimate the burden of the disease. In addition, the frequency of the disease varies geographically, with particular regions (Asia and Africa) having a higher prevalence than other areas of the world.[6] Several factors place transplant patients at greater risk of developing active TB.

A previous TB infection increases the likelihood of TB developing after transplantation.[5] The RESITRA (Spanish Network of Infection in Transplantation) cohort documented a relative risk of 4.3 for the development of symptomatic TB when the purified protein derivative (PPD) test was positive instead of negative.[4] In a systematic review of 139 cases of active TB infection after liver transplantation, 37% had a positive tuberculin skin test (TST), 23% had abnormal pretransplant chest imaging, and 13% had a history of untreated/improperly treated TB.[7] The number of pretransplant patients with a positive TST underestimates the number of patients infected with TB because end-stage liver disease may result in cutaneous anergy, which decreases the sensitivity of the

Abbreviations: BCG, Bacille Calmette-Guérin; LTBI, latent tuberculosis infection; PPD, purified protein derivative; QFT, QuantiFERON-TB Gold; TB, tuberculosis; TST, tuberculin skin test.

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TST. Chest radiography findings consistent with TB (ie, a military pattern, cavitary lesions, and upper lobe focal infiltrates) appear to be the single most important risk factor associated with the development of early-onset TB.[3]

The intensity of the immunosuppression (specifically the use of muromonab-CD3 and anti–T lymphocyte antibodies) plays an important role in the development of active TB.[5,6] Other risk factors include preexisting conditions that may affect immune function, such as chronic liver disease, diabetes mellitus, coinfections (cytomegalovirus, *Pneumocystis jiroveci*, and *Nocardia*), and allograft rejection.[3–5] In Spain, older age appears to increase the risk of posttransplant TB. This association may be relevant to countries such as Spain that are experiencing a decrease in TB cases in the general population; this suggests that older individuals may be more likely to harbor latent TB than younger persons.[4,6] Although posttransplant acquisition (donor-derived or nosocomially transmitted) is infrequent, it has been reported in the literature.[2,8]

CLINICAL FEATURES

Most active TB cases are diagnosed within the first 12 months after transplantation.[2–4] In a large Spanish cohort, 95% of all TB cases occurred during the first year, with a median time of onset of 183 days after transplantation (range = 28-499 days).[4] Similarly to the general transplant population, 83% of all TB cases among liver transplant recipients occur within the first year with a median time to onset of 4 months, the majority of cases primarily being a result of disease reactivation.[2]

Extrapulmonary TB occurs more frequently in transplant recipients versus normal hosts. An older review of solid organ transplant recipients with *Mycobacterium tuberculosis* infection noted that 51% had pulmonary TB, 16% had extrapulmonary TB, and 33% had disseminated TB.[2] A more recent series documented only disseminated disease in 9.5% of patients.[4] Disseminated disease may occur more frequently when liver transplant patients have received muromonab-CD3.[2]

Extrapulmonary and disseminated TB can involve obscure locations with varied clinical presentations. The involvement of nearly every organ, including the liver, gastrointestinal tract, skeletal system, muscles, skin, orbit, central nervous system, renal and genitourinary tract, lymph nodes, pericardium, larynx, and adrenal glands, has been described.[2,3] Because the presentation may be distinct from that seen in normal hosts, high clinical suspicion and a thorough evaluation are necessary for the diagnosis of most cases of extrapulmonary and disseminated TB. Tissue biopsy may be critical for the establishment of the diagnosis.

Fever, night sweats, and weight loss are commonly observed symptoms.[2,9,10] In patients with pulmonary TB, chest radiographs vary and may include focal infiltrates (40%), a military pattern (22%), nodules (15%), pleural effusions (13%), diffuse interstitial infiltrates (5%), and cavitary lesions (4%). Nodular patterns are more common in non–renal transplant recipients.[2]

DIAGNOSIS

Latent TB

TST using PPD and interferon-γ release assays [QuantiFERON-TB Gold (QFT) from Cellestis and T-SPOT.*TB* from Oxford Immunotec, Ltd.] are the 2 types of tests available for the diagnosis of a latent tuberculosis infection (LTBI; Table 1). In the general population, these 2 tests have good concordance for detecting latent TB.[11] One study compared QFT to PPD testing in 153 chronic liver disease patients awaiting liver transplantation. Concordance between the 2 tests was 85.1% ($k = 0.60$), and this suggests that QFT was comparable to PPD for the diagnosis of latent TB in this population.[12] Another study comparing QFT to PPD testing in patients with chronic liver disease revealed fewer positive results with PPD testing.[13] Currently, there is no reported advantage for one test versus the other; but in normal hosts, interferon-γ release assays have the advantage of differentiating people whose positive skin test reflects prior vaccination against Bacille Calmette-Guérin (BCG) infection. Although this ability to differentiate TST positivity related to BCG immunization has not been studied specifically in liver transplant candidates, the assays are likely to have similar performance characteristics and therefore may be advantageous in patients with a history of prior BCG immunization. Patients with a remote history of BCG immunization who are TST-positive are more likely to be positive because of prior infection with TB rather than vaccination; consequently, the majority of TST-positive adults are likely to have latent TB. Moreover, it is notable that patients with chronic liver disease are less likely than those in the general population to be identified by either modality because of diminished cellular responses associated with cirrhosis.[14–16] Because both QFT and TST measure the cellular immune response to *M. tuberculosis*, testing with QFT is unlikely to be helpful in patients with a negative TST related to defective cellular immune responses.[11,12] The full evaluation of a patient with cirrhosis before liver transplantation should be thorough and include a detailed medical and exposure history and a review of chest radiography (see the section on the evaluation of transplant candidates and donors). In posttransplant recipients, the diagnosis of LTBI similarly involves the use of TST or interferon-γ release assay testing. Test sensitivity is diminished because of the use of immunosuppressants after transplantation; as a result, historical and radiographic evaluations may be especially critical.

Active TB

TB may be present as a latent infection (quiescent or asymptomatic) or an active infection. The diagnosis of active TB requires the isolation of *M. tuberculosis* and/or pathological confirmation with consistent

TABLE 1. Recommended Approach for the Diagnosis and Treatment of TB in Liver Transplantation Patients

	Diagnosis	Treatment
Pretransplant candidates and donors		
Latent	History: TB risk factors, exposures, and prior infection. Testing: TST or interferon-γ release assays (assay sensitivities may be reduced in patients with cirrhosis) and chest radiograph for the evaluation of evidence of past infection (eg, granulomas and apical scarring). Key points: The 2-step method may detect TB in patients with remote exposure via the booster effect. For deceased donors, obtaining a history from family members may be useful. Chest radiography may help to identify patients with a history of TB.	Drugs: Isoniazid daily for 9 months or rifampin daily for 4 months (before transplantation only). Key points: Patients with compensated cirrhosis should be considered for treatment. Patients with uncompensated cirrhosis should defer therapy to the period after transplantation. Patients with recent exposure to TB, radiographic evidence of previously healed TB, and low body weight are at increased risk of progressing to TB disease, so higher priority for early intervention should be considered.
Active	History: Varied symptoms depending on the presence of pulmonary or extrapulmonary disease. Testing: Chest radiograph. Invasive diagnostic techniques may be required, especially for patients with extrapulmonary disease. Key points: A definitive diagnosis requires the isolation of M. tuberculosis in a culture and/or pathological confirmation. All positive cultures should undergo antimycobacterial drug susceptibility testing.	Candidates: Patients with active TB should not undergo transplantation; exceptions might be considered for patients with well-controlled infections. If patients undergo transplantation during therapy, one should consider altering the regimen to exclude rifamycin. Donors: Active TB is a contraindication for transplantation.
Posttransplant recipients		
Latent	History: TB risk factors, exposures, prior infection, and donor TB status. Testing: TST or interferon-γ release assays. Key points: The sensitivity of testing is significantly reduced; negative tests do not exclude a diagnosis. The 2-step method may detect TB in patients with remote exposure via the booster effect. Chest radiography may help to identify patients with past infections.	Drugs: Isoniazid daily for 9 months. Key points: Recipients of donors with latent TB should receive a 9-month course of preventive therapy with isoniazid.
Active	History: Varied symptoms depending on which organ or organs are involved. Extrapulmonary disease may be seen. Testing: Chest radiograph. Invasive diagnostic techniques may be required. Key points: A definitive diagnosis requires the isolation of M. tuberculosis in a culture and/or pathological confirmation. All positive cultures should undergo antimycobacterial drug susceptibility testing.	Localized, nonsevere disease: The initial therapy should not include rifamycins, and maintenance agents should include isoniazid and ethambutol. The addition of pyrazinamide or levofloxacin may shorten the treatment length. Severe disease, disseminated TB, or resistant disease: Rifamycin treatment should be considered during the initial and maintenance phases. Key points: Rifampin can significantly decrease serum levels of calcineurin inhibitors, and rifabutin may be preferable, although calcineurin inhibitor levels will still be reduced. Close monitoring of calcineurin inhibitor levels is imperative with early dose increases recommended.

changes in tissue sampling, including granulomas and/or the presence of acid-fast bacilli (Table 1). TST and interferon-γ release assays should not be used because they have reduced sensitivity in this population and do not differentiate between latent and active disease. Transplant patients infected with TB have a high frequency of coinfections (cytomegalovirus, community-acquired pneumonia, urinary tract infection, *Nocardia*, and aspergillosis), with rates as high as 23%, and these may lead to the delayed diagnosis of TB in transplant recipients.[3]

The clinical features of active TB in transplant patients differ from those in the general population, and the manifestations will depend on the site or sites of infection. Pulmonary TB is most common and should be considered in patients with unexplained respiratory illnesses who have abnormal radiographs. In comparison with normal hosts, the typical findings of upper lobe involvement and cavitation may be less commonly noted, and patients may present with pulmonary nodules, bronchiectasis, or even lymphadenopathy.[2,6] The manifestations of extrapulmonary

disease are diverse; consequently, TB should be considered in any patient with unexplained fever, especially if the recipient or the transplant donor has previously been noted to have a documented or suspected untreated latent infection. In many cases, because of the increased incidence of extrapulmonary disease and the difficulty of isolating the organism in expectorated sputum, invasive diagnostic techniques may be required. Bronchoscopy, laparoscopy, tissue biopsy, and bone marrow evaluation may be required to make a diagnosis.[3,10] A definitive diagnosis requires the isolation of *M. tuberculosis* from a culture. With standard microbiological methods, *M. tuberculosis* may take up to 6 weeks to grow; as a result, the use of specialized media that enhance growth and molecular and genetic amplification techniques may be useful in patients for whom there is a high clinical suspicion of TB.[3,17] Once TB is identified, it is important for clinical isolates to be tested for susceptibility to available antimycobacterial medications. In some cases of active TB, cultures will be negative. Consequently, consistent pathological findings, including the presence of acid-fast bacilli or caseating granulomas, may be indications for the initiation of antituberculous therapy.

PREVENTION OF TB: EVALUATION OF TRANSPLANT CANDIDATES AND DONORS

Evaluation of Transplant Candidates

A thorough history documenting TB risk factors, exposures, and infections should be obtained from all transplant candidates.[5,6] This includes previous travel to endemic areas, institutional exposure, and contact with individuals with active TB (ie, household or workplace contacts).[5,6] Previous infections with TB, latent or active, should be recorded along with details about the treatment (or lack of treatment), medications, and length of therapy[5,6] (Table 1).

All transplant candidates should be evaluated for latent TB by either TST or interferon-γ release assays; this includes patients with a history of BCG vaccination.[5,6] Despite this recommendation, only 40.5% to 47% of transplant recipients are tested prior to transplantation.[2,4,5] There are limited data comparing TST and interferon-γ release assays in transplant candidates, and no gold standard exists to support the use of one test over the other. Because of the immunosuppressed state of most transplant candidates due to cirrhosis, a TST with ≥5 mm of induration at 48 to 72 hours is considered positive and reflective of past infection.[5,6] Patients with negative results should have a second TST in 1 to 3 weeks.[5,6,18] This 2-step method may identify patients with remote exposure to TB via the booster effect, by which the first TST stimulates the immune system and allows it to react to the second test.[18] Despite the use of the 2-step method, the potential to underdiagnose LTBI in this immunosuppressed population, which is at risk for cutaneous anergy, remains high. Anergy testing, aimed at identifying patients who can mount a delayed-type hypersensitivity response, is controversial, unpredictable, and generally not recommended.[18] In anergic patients, serial TSTs will not result in a positive skin reaction. The proportion of patients falling into this category is unknown, and this has important treatment implications. It is unknown which patients with negative testing will be most likely to benefit from treatment for latent TB. Patients with radiographic findings or a clinical history highly suggestive of prior untreated TB should be assessed on a case-by-case basis for the treatment of latent TB, and consideration should be given to the risk of the treatment versus its benefit. Patients who are not treated should be closely followed for potential reactivation. Further research and improved diagnostic assessments are needed in this area.

An individual should not undergo TST or interferon-γ release assay testing only if he has a well-documented history of previous TB infection or a positive TST in the past.[5,6] A patient with a positive test should undergo chest radiography and a symptom review to rule out active TB.[5,6] Active TB is a contraindication for transplantation,[5] although exceptions might be considered for patients on treatment with a well-controlled infection, especially if they have progressive liver failure related to antituberculous medication.

Evaluation of Transplant Donors

M. tuberculosis infections have been transmitted through liver transplant grafts.[5,19] Because of this risk, all living donors should undergo an evaluation similar to that used for transplant candidates; it should include a careful history and TST or interferon-γ release assay testing, particularly in areas with a high prevalence of TB, such as Asia and Africa[5,6,20] (Table 1). Centers for Disease Control and Prevention guidelines should be used in interpreting TST results, whereas QFT and T-SPOT.*TB* should be read according to the manufacturers' instructions.[6] The challenge is accurately diagnosing TB infections in deceased donors, who provide organs for more than 95% of all liver transplants and for whom only limited relevant historical information, including previous tuberculin testing, is often available.[21] Obtaining a TB history from family members and relatives may be useful.[6] Living donors with LTBI should be considered for treatment.[6] Treatment should be expedited for patients with recent TST conversion and/or TB exposure because these patients are at greater risk for developing active TB.[6] Treatment regimens are similar to those recommended for the general population (see the section on latent TB treatment). The length of therapy prior to liver donation has not been well studied, and further investigation is required to determine if a subset of patients can be treated with a shorter course prior to donation under the assumption that the recipients will be treated after

transplantation. In the case of transplantation using organs from deceased donors, it is more difficult to assess the presence of latent TB. All donors should undergo screening with detailed histories and chest radiographs. Because historical information for donors is often incomplete, the risk of donor-derived TB may be underestimated. Donors from areas in which TB is more prevalent and those with probable TB exposure (defined as known close contact or a high-risk living environment such as prison) should be carefully scrutinized for evidence of both active and latent TB. In these cases, whenever it is possible, respiratory and urine cultures should be collected.[5] In addition, any enlarged lymph nodes in the surgical field should be biopsied and cultured for *M. tuberculosis*.[5] Because this is not part of the usual donor acquisition evaluation; the recipient institution should make a specific request. Additionally, the finding in a recipient of unexpected TB thought to be possibly of donor origin should prompt notification of the local organ procurement organization and subsequent communication with transplant centers caring for other recipients of organs from the same donor to facilitate the evaluation for potential donor-derived TB.

Organs from donors with active TB or with a high suspicion of active TB should not be used.[6] Recipients of organs from donors with latent TB should receive a 9-month course of preventive therapy with isoniazid (see the section on latent TB treatment).

TREATMENT

Latent TB

Transplant recipients with LTBI are at increased risk of developing active TB. Reactivated TB may be difficult to diagnose in transplant patients, pose a potential public health safety risk, and increase the potential for serious morbidity and mortality.[6] For these reasons, the treatment of LTBI is generally recommended. Liver transplant candidates and recipients present a unique challenge because of the potential risk of hepatotoxicity associated with therapy.

The standard therapy for treating LTBI in the general population is isoniazid daily for 9 months.[22] Alternative regimens include isoniazid twice weekly via directly observed therapy for 9 months, isoniazid daily for 6 months, and rifampin daily for 4 months.[22] Concerns about hepatotoxicity secondary to the use of these agents have prompted some experts to recommend delaying treatment for LTBI until the period after liver transplantation. This differs from the recommendations for other solid organ transplant candidates, such as kidney and lung transplant candidates, for whom the treatment of latent TB is recommended before transplantation whenever this is possible.[5,6] If treatment is delayed until the period after transplantation, rifampin should be avoided because of interactions with calcineurin inhibitors. The initiation of posttransplant preventive treatment should begin as soon as a patient's liver function has stabilized to prevent the development of reactivated diseases.

Recent studies have shown that LTBI treatment can be safely used in select liver transplant candidates.[6,23,24] One study compared 18 liver transplant candidates (mean Child-Pugh score = 8) who received 12 months of isoniazid treatment for LTBI to matched controls; no difference in hepatic function tests was noted between the 2 groups, and none of the 18 cases had to discontinue therapy.[23] Another study reported similar findings and noted the safe use of either 9 months of daily isoniazid or 4 months of daily rifampin in 14 liver transplant candidates (mean Child-Pugh score = 6).[24] Given these findings, we recommend that transplant candidates with compensated cirrhosis be considered for the treatment of LTBI with close monitoring for treatment-related toxicity, whereas patients with decompensated disease should defer therapy until the period after transplantation when their liver function is more stable (Table 1).

There are no studies evaluating the safety of transplantation for individuals who are in the midst of treatment for LTBI, and it is unknown if these individuals are at risk for worse outcomes because of activation of TB or drug toxicity in the new liver. Because of the relative effectiveness of LTBI treatment, the tolerability of isoniazid in the transplanted liver, the limited availability of acceptable donor organs, and the high rate of death for patients on the waiting list, it is reasonable to consider transplantation for patients receiving LTBI treatment. The standard duration of treatment should be completed.

It should be recognized that patients with recent exposure to TB (new TST conversion), radiographic evidence of previously healed TB, and low body weight are at increased risk of progression from LTBI to TB disease.[18] These individuals deserve special consideration and should receive treatment as soon as it is medically possible.

Once therapy is started, liver enzymes should be monitored frequently; experts suggest checking liver function tests every 2 weeks for 6 weeks and then monthly.[6] In the general population, guidelines recommend stopping therapy if the enzymes are elevated 3-fold and the patient is symptomatic or if there is a 5-fold elevation without symptoms.[18] No guidelines for discontinuing therapy have been established in the liver transplant population. An elevation in liver enzymes does not necessarily reflect drug toxicity because a number of conditions may manifest in a similar manner. Liver biopsy may be needed to clarify the underlying ideology. In patients with significant hepatotoxicity, some experts recommend that levofloxacin and ethambutol for at least 6 months be considered, although there are no controlled trials of this treatment.[2,3,5]

Active TB

The American Thoracic Society, the Centers for Disease Control and Prevention, and the Infectious

Diseases Society of America recommend 4 regimens for the treatment of pulmonary TB.[22] These regimens include a 2-month intensive phase followed by a continuation phase of 4 to 7 months.[22] In the liver transplant population, recommendations for treating active TB differ because of the known risk of drug-drug interactions between antituberculous medications and immunosuppressive agents and the potential for hepatotoxicity associated with first-line TB therapy.[5,6] These differences also have an impact on the suggested length of treatment.[5,6]

Isoniazid, rifampin, and pyrazinamide can all cause hepatotoxicity.[17,22] The deleterious effect on the liver is increased when these agents are used in combination rather than alone.[5,6] In a large Spanish series, 12 of 24 liver transplant recipients with TB (50%) developed hepatotoxicity during treatment.[25] Another major challenge in treating TB in transplant patients is the use of rifampin, which can significantly decrease serum levels of calcineurin inhibitors and mammalian target of rapamycin inhibitors and alter corticosteroid metabolism.[3,5,6,17] For this reason, rifamycins must be used with extreme caution in transplant recipients. Cyclosporine and tacrolimus doses should be increased 3- to 5-fold at the outset of therapy, and levels should be monitored closely.[5,26] However, even with this adjustment and careful monitoring, combining rifampin and calcineurin inhibitors can lead to increased graft rejection, graft loss, and TB-related mortality.[5] Rifabutin appears to be as effective as rifampin, but it is a weaker inducer of cytochrome P3A4 and therefore results in less intense drug interactions.[6,22,27] Little data exist on its use in the transplant population, but it appears to be just as efficacious as rifampin in human immunodeficiency virus–infected patients and may be considered an alternative in situations in which the use of a rifamycin is mandatory.[5] If rifabutin is used, cyclosporine and tacrolimus doses should be increased upon the initiation of therapy, and calcineurin inhibitor levels should be monitored closely. Because of the risks of administering rifamycins in transplant recipients, many clinicians opt to avoid these medications in transplant recipients for whom alternative regimens are feasible.

Fluoroquinolones and aminoglycosides are other agents used in the treatment of TB; they are primarily used in cases of multidrug resistance or intolerance of first-line medications. Patients on aminoglycosides, such as streptomycin, amikacin, and kanamycin, should be monitored closely for nephrotoxicity (especially with calcineurin inhibitors) and ototoxicity.[22] Fluoroquinolones, notably levofloxacin and moxifloxacin, are frequently used in the treatment of drug-resistant TB.[22] The prolonged use of these agents may result in arthralgias, which typically resolve once the drug has been discontinued.[3] Because of a more favorable side-effect profile versus rifampin and aminoglycosides, fluoroquinolones have been increasingly considered in transplant recipients.[3,22]

The treatment of active TB in transplant recipients is based on expert opinion, and no randomized clinical trial data are available[3,5] (Table 1). In cases of localized, nonsevere disease, attempts should be made to avoid rifamycins in initial therapy, and maintenance agents should include isoniazid and ethambutol for 18 months. The addition of pyrazinamide or levofloxacin may shorten the treatment length, but patients should be closely monitored. Some experts prefer to use a rifamycin; in that case, 9 months of therapy is sufficient. Patients with severe disease, disseminated TB, or suspicion or evidence of resistance to isoniazid should be considered for rifamycin treatment during the initial and maintenance phases. Multidrug-resistant TB may require the use of 4 to 6 agents for a prolonged period of time and should be managed only in consultation with an infectious diseases specialist.[22]

The ideal length of therapy remains controversial, and it is affected by the extent of the disease, choice of regimen, response to therapy, and resistance profile of the organism. Some experts suggest that bone and joint involvement, central nervous system disease, and disseminated TB require longer treatment.[6] In addition, patients with cavitary pulmonary TB who remain culture-positive after 2 months of therapy require longer treatment. In general, many providers recommend 12 to 18 months of anti-TB treatment.[3,5,17,20]

In conclusion, TB is a serious infection in the transplant population. In particular, liver transplant patients have a poor prognosis. The mortality rate has been as high as 30% to 100% in various series.[3,17] In addition, allograft rejection is a serious result of either a planned or drug-induced reduction of immunosuppressive therapy.[17] Experience with antituberculous therapy in the liver transplant population is necessary to prevent mortality and organ rejection. Future research should focus on developing rapid, sensitive, and specific diagnostic tests, new therapeutic drugs with fewer side effects, and shorter treatment strategies for transplant patients.

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