

Leprosy-tuberculosis co-infection: A case series

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Abstract

Background: Leprosy and tuberculosis (TB) share common characteristics, such as acid-fastness of causative bacteria, geographic endemicity, route of spread, large number of asymptomatic infections, and requirement of multiple drugs for long periods of time to prevent resistance and provide treatment. Being relatively common, co-infection with the two diseases should occur based on chance alone. However, coinfection is surprisingly rare, with less than 20 cases being reported in the last decade.

Aim: The purpose of this case series was to study the clinico-epidemiological profile of patients with leprosy and TB co-infection.

Methods: This prospective, descriptive, case series describes leprosy patients with a past or current diagnosis of TB who visited the leprosy clinic of a tertiary care hospital over 3 years. The demographic details of the patients, details about the type of leprosy, slit skin smear, lepra reaction, and use of corticosteroids were noted for all patients. The type of TB, chest X-ray findings, sputum positivity, Interferon gamma release assay (IGRA) test, and Mantoux test results were recorded. The gap between the two diagnoses, the first disease to be diagnosed, family history of either disease, and the presence of predisposing factors were noted.

Results: This case series describes a total of 20 patients with leprosy co-infected with TB. There were 11 (55%) males, and the mean age of patients was 32.7 years. Half of these patients had lepromatous leprosy, and a similar number had type 2 lepra reaction. Pulmonary TB was seen in 12 (60%) patients, and tubercular pleural effusion in two (10%) patients. Multidrug-resistant TB was seen in two patients, and only one patient had received the bacilli of Calmette-Guerin (BCG) vaccination. Of the two diseases, leprosy was diagnosed first in six (30%) patients, while it was TB in 12 (60%) patients, and two (10%) patients had a concomitant diagnosis.

Limitations: The small number of patients in this single-centre study from a tertiary care hospital may not be reflective of the general population.

Conclusion: Leprosy and TB co-infection may present several management issues involving diagnosis and treatment, including drug resistance to tubercular bacilli. Management guidelines for such coinfections are needed to facilitate treatment of such patients and prevent high mortality and morbidity associated with such coinfections. More studies are needed to correctly define the clinico-epidemiological parameters of patients with co-infection.

Key words: BCG, coinfection, leprosy, Hansen's disease, tuberculosis

Introduction

Leprosy and tuberculosis (TB) are granulomatous disorders caused by acid-fast bacilli, namely *Mycobacterium leprae*

and *Mycobacterium tuberculosis*, which share several characteristics. Both are predominantly transmitted via aerosols but can manifest cutaneously. Both are endemic in

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similar geographic locations, and clinical manifestations are apparent in only a small proportion of infected individuals.¹ Multiple drugs are needed to treat the two diseases for a considerable period of time to achieve a cure.

India has a high burden of leprosy and TB. Based on chance alone, the number of individuals with concomitant infection of the two diseases must be high. Further, the use of corticosteroids to treat reactional leprosy may predispose to the development of TB due to immunosuppression. However, co-infection with the two diseases is rarely reported in the literature.² This has been attributed to various factors, such as the differential rate of growth of the mycobacteria and possibly cross-immunity. Only case reports of such co-infections exist in the literature, with no more than 20 cases being described in the last decade or so.³ Co-infected individuals form a special group of patients as they are said to be associated with an increased mortality and high morbidity.⁴ Further, several management issues arise from such co-infections, which have been discussed in this article.

The aim of this study was to study the clinico-epidemiological profile of patients with leprosy and TB co-infection.

Methods

This prospective, descriptive, case series describes patients from a tertiary care hospital in North India over 3 years, from April 2021 to March 2024. The study was approved by the Institutional Ethics Committee of the hospital. All patients of leprosy attending the leprosy clinic in the dermatology outpatient department with concomitant or past diagnosis of TB were enrolled for the study. The diagnosis of leprosy was made by the dermatologist based on WHO guidelines which includes the presence of at least one of the three cardinal signs: (i) hypopigmented or erythematous patch or plaque with definite loss of sensation (ii) thickened peripheral nerve with sensory/motor/autonomic deficit in its distribution and (iii) presence of acid-fast bacilli in slit skin smear. Additionally, classification of leprosy was done based on clinical features and skin biopsy. The diagnosis of TB was made by the respective specialist based on clinical features and investigations, which varied from case to case. Mere presence of acid-fast bacilli (AFB) in sputum was not sufficient for the diagnosis of pulmonary TB if the patient already had leprosy. If pulmonary TB was suspected, then confirmation of diagnosis was done using line probe assay or cartridge based nucleic acid amplification test (CB-NAAT).

The patients' demographic profile, such as age, sex, address, and occupation, was noted. Body mass index and hemogram were evaluated for the assessment of the nutritional status of the patients. All patients selected for the study were evaluated for the type of leprosy, slit skin smear positivity, duration of multidrug therapy, and number and type of lepra reactions and their management, including the use of corticosteroids or other immunosuppressive agents. Records of the type of TB,

duration of TB, sputum positivity, interferon gamma release assay (IGRA) results, and status of anti-tubercular therapy were noted. Wherever possible, drug resistance studies for TB were done. The gap between the two diagnoses, the disease which was diagnosed first, and the Bacillus Calmette Guerin (BCG) immunisation status were recorded. Their general condition, including nutritional status and the presence of other co-morbid conditions such as diabetes mellitus, was recorded. The patients were also asked about having any family member suffering from TB and/or leprosy.

Results

A total of 20 patients having leprosy and TB co-infection were recorded during the study period. There were 11 (55%) males and nine (45%) females. The age of the patients ranged from 16 years to 65 years, with the mean age being 32.7 years.

The clinical profile of leprosy as per the Ridley-Jopling classification has been given in Table 1. Half of all patients were classified as lepromatous leprosy, and a similar number had type 2 lepra reaction. Slit skin smear was positive in 14 (70%) patients.

The type of TB in the patients has been presented in Table 2. An overwhelming 70% patients had pulmonary TB, which included 10% patients with tubercular pleural effusion. Chest X-ray features suggestive of TB were seen in 15 (75%) patients. Sputum showed the presence of acid-fast bacilli in 07 (35%) patients only. The IGRA test was positive in 09 (45%) of these patients. A total of 12 (60%) patients showed a positive reaction to the tuberculin antigen (Mantoux test). A history of BCG vaccination was present in only one (05%) of our patients. All patients were subjected to drug

Table 1: Distribution of patients according to type of leprosy

Type of leprosy	Number (Percentage)
Tuberculoid leprosy (TT)	0 (0%)
Borderline tuberculoid leprosy (BT)	4 (20%)
Mid-borderline leprosy (BB)	1 (5%)
Borderline lepromatous leprosy (BL)	5 (25%)
Lepromatous leprosy (LL)	10 (50%)
Type 1 reaction	4 (20%)
Type 2 reaction	10 (50%)

Table 2: Distribution of patients according to type of tuberculosis

Type of tuberculosis	Number (Percentage)
Pulmonary tuberculosis	12 (60%)
Tubercular pleural effusion	2 (10%)
Abdominal tuberculosis	1 (5%)
Lymph node tuberculosis	1 (5%)
Tubercular tenosynovitis	1 (5%)
Pott's spine	1 (5%)
Scrofuloderma	1 (5%)
Tuberculosis of the fallopian tubes	1 (5%)

resistance studies for TB, and two (10%) showed resistance to rifampicin. Both of these patients were on multidrug therapy for leprosy. Of these two, one was being treated for lepra reaction with corticosteroids. The other had a history of TB and had received an incomplete course of anti-tubercular therapy 3 years back. While the former had resistance to rifampicin only, the latter developed resistance to both rifampicin and isoniazid (*KatG* gene mutation only). They were treated with the shorter oral bedaquiline-containing Multi drug resistant TB (MDR-TB) regimen. This regimen includes an intensive phase of 6 months of bedaquiline, levofloxacin, clofazimine, pyrazinamide, ethambutol, high-dose isoniazid, and ethionamide, followed by the 5-month continuation phase of levofloxacin, clofazimine, ethambutol, and pyrazinamide. Both responded favourably to treatment. Family history of TB was positive in six (30%) patients, while none of the patients with leprosy had any family member affected with leprosy. The precipitating factors of TB were presumed to be corticosteroids in five (25%) patients and malnutrition in three (15%) patients. All these patients were on corticosteroids for the treatment of lepra reaction. There were no patients with other predisposing factors, such as diabetes mellitus and immunosuppressives.

Leprosy was diagnosed first in 06/20 (30%) patients, while TB was diagnosed first in 12/20 (60%) patients. In two (10%) patients, both diseases were diagnosed concomitantly. The gap between the two diagnoses has been summarised in Figure 1. A brief summary of the clinical profile of the individual patients has been presented in Table 3. Figure 2

shows a patient of leprosy with multiple hypopigmented patches over the trunk while Figure 3 shows radiographic changes in a patient of pulmonary tuberculosis.

Discussion

Both leprosy and TB are infections known to man for millennia. However, their co-infection was first reported. Both bacteria share some common antigens. They occur due to impaired cell-mediated immune response, and a common genetic predisposition leading to impaired immunity has been postulated as the reason behind dual infections.¹ Low cell-mediated immune response may be the reason for the occurrence of co-infection in patients with multibacillary

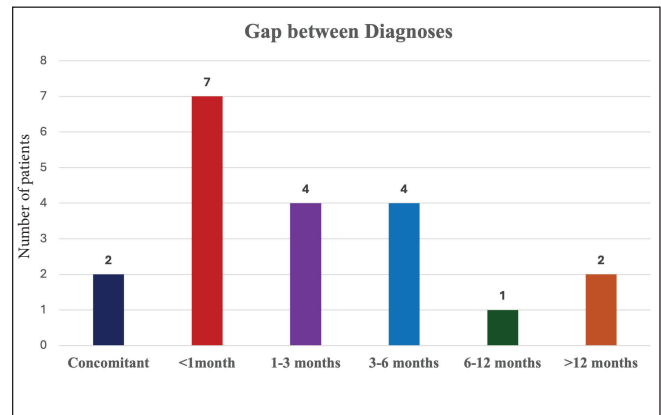


Figure 1: Time gap between diagnoses of leprosy and tuberculosis in co-infected patients.

Table 3: Details of the patients with leprosy and tuberculosis co-infection

S. No.	Age/Sex	Leprosy type	Lepra reaction	Tuberculosis (TB) type	First diagnosis	Gap between diagnoses	BCG status
1.	18/M	LL	T2	Pleural effusion	TB	1 month	N
2.	25/F	LL	T2	Pulmonary TB	HD	15 months	N
3.	45/M	BB	T1	Pulmonary TB	HD	1 week	N
4.	25/F	LL	T2	Pulmonary TB	TB	3 months	N
5.	35/M	BL	T2	Pulmonary TB	TB	1 month	N
6.	28/F	LL	T2	Pulmonary TB	HD	8 months	N
7.	45/F	LL	T2	Scrofuloderma	Concomitant	-	N
8.	60/M	LL	T2	Lymph node TB	Concomitant	-	N
9.	22/M	BT	T1	Pulmonary TB	TB	1 month	N
10.	20/F	BT	-	Pott's spine	TB	4 months	N
11.	25/F	BT	T1	Fallopian tube TB	TB	1 month	N
12.	28/F	BL	-	Pulmonary TB	HD	5 months#	N
13.	21/M	BL	-	Pulmonary TB	TB	3 years*#	N
14.	35/F	LL	T2	Pulmonary TB	TB	6 months	N
15.	32/M	LL	-	Pleural effusion	TB	2 months	N
16.	50/M	BL	T2	Abdominal TB	HD	3 months	N
17.	65/F	BL	-	TB Tenosynovitis	TB	1 month	N
18.	23/M	LL	T2	Pulmonary TB	TB	6 months	N
19.	16/M	LL	-	Pulmonary TB	TB	2 months	N
20.	36/M	BT	T1	Pulmonary TB	HD	1 month	Y

* MDR TB * Developed MDR TB again after 4 months of MDT for leprosy. M: Male; F: Female; BT: Borderline tuberculoid leprosy; BB: Mid-borderline leprosy; BL: Borderline lepromatous leprosy; LL: Lepromatous leprosy; T1: Type 1 lepra reaction; T2: Type 2 lepra reaction; TB: Tuberculosis; HD: Hansen's disease; N: No; Y: Yes

leprosy. This theory is, however, controversial as leprosy has pathogen-specific energy. The rare association of the two diseases has been attributed to cross-immunity between the two diseases. The variable growth rate of the two bacteria and transmission dynamics are also attributed to co-infections being reported rarely.⁵ This is evident from the low rates of leprosy in TB-endemic areas. Others argue that patients with leprosy are more susceptible to TB, but TB, being a more aggressive disease, leads to mortality and may have historically led to reduced burden of leprosy.⁶ Common genetic susceptibility may be the reason in patients with co-infection. However, in studies no difference between

CD4, CD8, B-cells, or IL-12/23 was observed in co-infected patients.⁷

BCG vaccination for TB also offers protection against multibacillary leprosy up to the tune of 98%.⁸ In our study, we found that none of the patients, except one, had received the BCG vaccine. Malnutrition and the use of steroids for lepra reactions are also considered predisposing factors for the development of TB. This was also seen in a considerable number of our patients. Apart from this, the social impact of leprosy is also considered a factor in the development of TB,⁹ which we did not assess. Immunosuppressive agents,



Figure 2: A patient of leprosy with multiple hypopigmented hypoesthetic patches over the trunk.

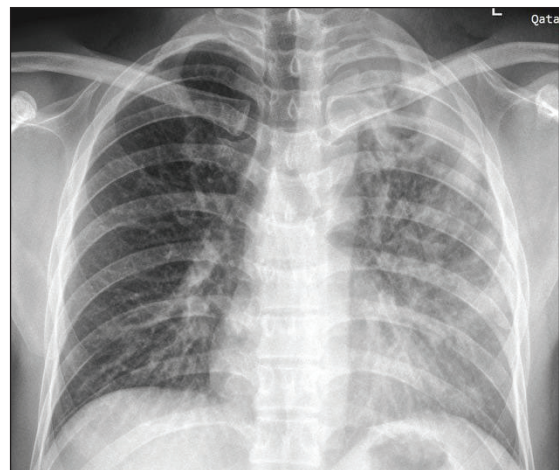


Figure 3: Chest X-Ray of a patient with pulmonary tuberculosis showing non-homogeneous opacity in the left lung with multiple cavitary lesions in the upper lobe of the left lung.

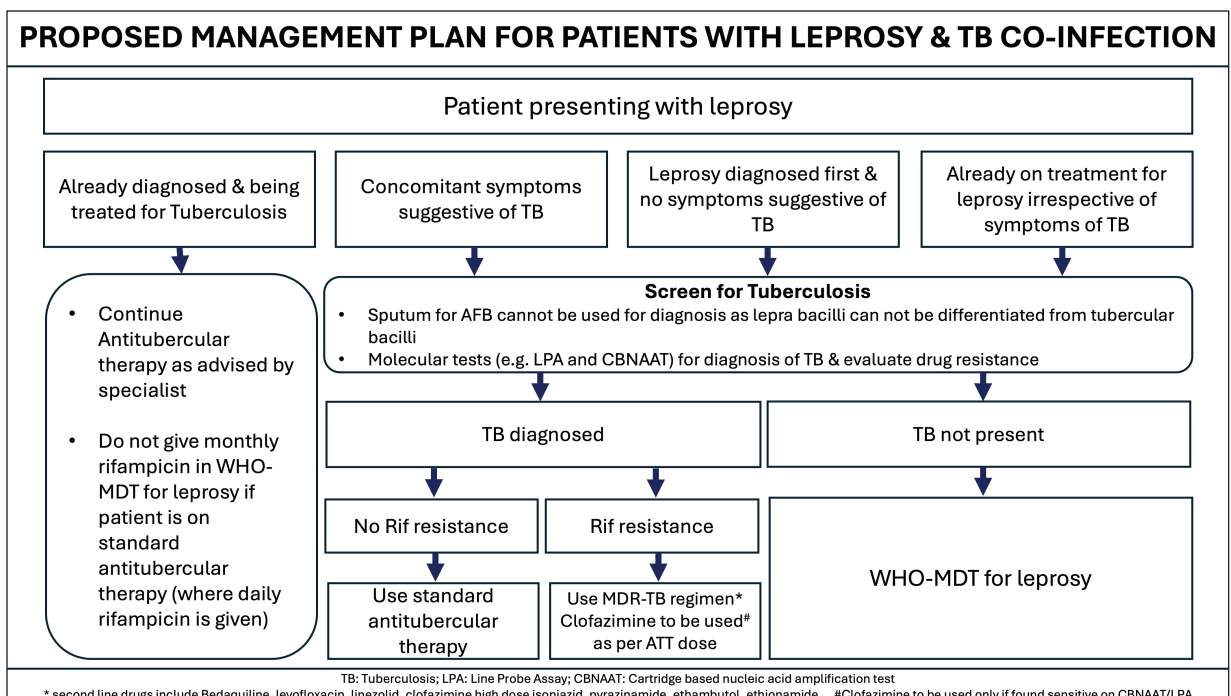


Figure 4: Proposed management plan for leprosy patients with tubercular co-infection.

diabetes mellitus, and renal disease are other predisposing factors.

Similar to our findings, previous studies have found that co-infection is more commonly seen in males and in the fourth decade of life.⁶ Males have a higher chance of developing both leprosy and TB than females, due to socio-behavioural factors (such as greater social contacts and high-risk occupations) and genetic factors. Though tubercular infection is more commonly seen in patients at the lepromatous pole, it occurs throughout the spectrum of leprosy. We found that half our patients had lepromatous leprosy, suggesting the role of cell-mediated immunity in co-infection. Rajagopala *et al.*⁶ found that more than 90% patients out of 122 included in the systematic review were affected with pulmonary TB, while Cavalcante *et al.*³ found 61.1% patients affected with pulmonary TB, which is similar to the figure in our study (70%). This difference could be due to the number of patients in the studies or geographic variations.

Most case reports and reviews suggest that leprosy is more commonly diagnosed first in patients with co-infection.^{1,3,6,10} Contrarily, we found TB was the first diagnosis in 60% of the patients. It is important to note that in 45% patients, the diagnosis was made either concurrently or within a month of diagnosis of either condition. This may suggest a mycobacteria-specific anergy as a predisposing factor.¹¹ It is worth noting that TB itself may act as a trigger for lepra reactions.¹²

The twin infections present unique diagnostic and management issues. Sputum of patients with multibacillary leprosy may show AFB, and it is not possible to differentiate the two bacilli on microscopy.¹³ Protein homologs of *Mycobacterium leprae* may cross-react with T-cell response in protein-based tests such as IGRA and confound results.¹⁴ Additionally, the tuberculin test may show giant strong reactions in patients with multibacillary leprosy.¹⁵ Thus, results must be interpreted with caution, and if needed, molecular methods and culture must be employed for diagnosis of TB.¹

The use of monthly rifampicin as a part of therapy for leprosy in a patient with yet undiagnosed TB may lead to the development of resistance and reduced effectiveness of anti-tubercular therapy later.¹⁶ Clofazimine is also weakly bactericidal for *Mycobacterium tuberculosis* and is employed in second-line antitubercular regimens, albeit at a higher dose. Its use for leprosy may lead to sputum culture negativity and complicate the management of MDR-TB.⁴ A proposed algorithm for the management of cases of leprosy with tubercular co-infection has been outlined in Figure 4.

Limitations

This was a descriptive case series. We need more analytical studies from multiple centres and on a larger number of patients to assess the actual gravity of the co-infection. Further, the findings are from a tertiary care hospital and may not be applicable to the general population.

Conclusion

Dermatologists must keep the possibility of TB in mind when managing patients with leprosy. Screening for TB is recommended in all patients with leprosy. Switching to minocycline-based regimens is an option if TB has not been ruled out. Further, drug resistance testing for TB may be done in all patients with co-infection, if they have been given monthly rifampicin for leprosy. Given that corticosteroids for lepra reactions may predispose to TB, the use of alternative drugs for managing lepra reactions should be encouraged. The nutritional status of leprosy patients must be assessed and taken care of. BCG vaccination must be given to all patients with leprosy. Further studies are warranted to get the complete clinico-epidemiological picture of the co-infection. Proper guidelines regarding the management of such infections are the need of the hour.

Ethical approval: The research/study was approved by the Institutional Review Board at J N Medical College, AMU, number IECJNMC/752, dated 20/03/2021.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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