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**RESEARCH ARTICLE**

# EPIDEMIOLOGY OF TUBERCULOSIS IN LEPROMATOUS LEPROSY PATIENTS IN TAMIL NADU, INDIA: A CASE STUDY

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**ABSTRACT**

*Mycobacterium leprae* (*M. leprae*) and *Mycobacterium tuberculosis* (*M. tuberculosis*) cause leprosy and tuberculosis respectively are considered chronic pathogens causing disease that take months sometimes year‘s to develop and without treatment eventually result in death. Lepromatous leprosy individuals have tuberculosis as co-infection, which means one organism weakens the patient and reduces the ability of the immune system to respond adequately or rapidly enough and this allows a more virulent organism to infect the patient some time lepromatous leprosy patients were well protected from tuberculosis infection by cross immunity. In this context the 73 lepromatous leprosy patients from leprosy rehabilitation centre were screened for tuberculosis as co-infection. The prevalence of oral pathogens among lepromatous leprosy patients shows the presence of *Staphylococcus sp* (30%) as predominant followed by *Bacillus sp* (23%), *Streptococcus sp* (21%), and Diplococci- *S. pneumoniae* (1%). The dominant of *Staphylococcus sp* in the sputum specimens of lepromatous leprosy patients shows that they were suffering from respiratory infections such as sinusitis, pneumonia, tonsillitis and pharyngitis.



## INTRODUCTION

*Mycobacterium leprae* (*M. leprae*) and *Mycobacterium tuberculosis* (*M. tuberculosis*) cause leprosy and tuberculosis respectively are considered chronic pathogens causing disease that take months sometimes years to develop and without treatment eventually result in death. Leprosy popularly through to be a disease of the past and World health organization (WHO) 2010 report reveals that 228, 474 new cases of leprosy reported throughout the world annually. WHO leprosy transmission report reveals that exact mechanism of transmission of leprosy is not known. The widely held belief was that the leprosy may be transmitted by contact between cases of leprosy and healthy persons or even by respiratory route, but the mode of transmission still remains a mystery. Leprosy is a neurological disease that mainly accumulate in the extremities and inhabits macrophages through which it infects the Schwann cells lead to a nerve damage and sensory loss (Hansen 1973). There are two forms of leprosy such as tuberculin and lepromatous leprosy. Lepromatous leprosy is the more contagious form in which the body is unable to mount a resistance and the bacterium freely multiplies in the skin causing nodules to appear all over the body and face. It also infects the mucous membrane of the nose and throat creating a rather disturbing physique. Tuberculin leprosy (TL) causes an immune defence in which the body cells crowd around the invading organisms in deep skin layer which causes hair follicle, sweat glands and nerve ending at the site to be destroyed. The skin then becomes dry and discoloured and loses feeling. Leprosy exists as tuberculoid and lepromatous leprosy with a range intermediate cases. In lepromatous leprosy large number of bacilli is found in the lesions and has higher titre of circulating antibody against several *M. leprae* antigens. In tuberculoid leprosy there are fewer bacilli and the individuals show marked cell mediated immune response.

Both leprosy and tuberculosis were prevalent in Europe during the first millennium but thereafter leprosy declines. It is not clearly known but the cross immunity may protect tuberculosis patients from leprosy (Lietman et al., 1997). The derived amino acid sequence of the *M. tuberculosis* and *M. leprae* proteins showed 85% identity (Donoghue et al., 2005). In Nigeria 71.4% of patients have tuberculosis, 75% have multi-bacillary leprosy and they were HIV seropositive. This emphasizes the need for careful sample selection in studies involving HIV and tuberculosis / leprosy and for careful monitoring of the HIV / leprosy interaction (Awofeso et al., 1995). The lepromatous leprosy patients have no or very little immune resistance to the *M. leprae*. They are not able to mount a response because of a lack of cell mediated immunity such infected leprosy individuals have very poor immune status and nutritional status. The lepromatous leprosy patients

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have severe weight loss, loss of appetite and reduction of skin fold thickness. The infected individual's level in sera of diet dependent proteins such as albumin and retinol binding protein are significantly decreased. The leprosy patients have low level in haemoglobin and reduction in serum iron and zinc concentration therefore the low status of macro and micronutrients in such leprosy individuals would trigger the co-infection of tuberculosis. The lepromatous leprosy were characterized by defective granulomas with lowered T-cell and macrophage mediated response, this in turns lower the immunity and may allow co-infection of *M. tuberculosis* infection. (Donoghue, 2005) reported that the earliest case of co-infection of both leprosy and tuberculosis was found by the researchers in the DNA from a body discovered in a 1st century CE burial cave in Jerusalem. Many of the lepers died of tuberculosis until there were too few of them to further spread leprosy. In a study in French Polynesia, tuberculosis in leprosy patients detected between 1902 and 1991 reveals that mortality from tuberculosis in leprosy patients detected between 1901 and 1930 was 20.7%, and decreased to 8.04% in patients detected from 1931 to 1959. In total, it was estimated that 26.4% of the leprosy cases had developed tuberculosis. From 1960 to 1991, 350 new cases of leprosy were detected (141 MB, 209 PB). Of them, 12 (3.4%) developed tuberculosis (7 before detection of leprosy, 5 after detection of leprosy). The author further reports that lepromatous patients could share factors of susceptibility to mycobacterium diseases with patients developing tuberculosis (Glaziou *et al*., 1993). Lepromatous leprosy individuals have tuberculosis as co-infection which means one organism weakens the patient and reduces the ability of the immune system to respond adequately or rapidly enough and this allows a more virulent organism to infect the patient (Abel *et al.,*1998; Sapkota 2007). In this context lepromatous leprosy patients at Pudupatti were screened for the prevalence of tuberculosis as co-infection were studied and the prevalence of oral infection were also recorded.

## MATERIALS AND METHOD

### Selection of the study population

Leprosy Rehabilitation centre is located at Pudupatti which is a village in Madurai East Taluk, Madurai District, Tamil Nadu, South India. Pudupatti is 10.3 km far from its Taluk Main Town Madurai East. Pudupatti is located 9.4 km distance from its District Main City Madurai East. It is located 410 km distance from its state main city Chennai. The geographical location of Madurai is 9.91 N, 78.1 E. It is located at an altitude of 100.58 meters (330 feet) above sea-level. About 216 leprosy infected individuals are living in this leprosy rehabilitation centre. Among them 150 were lepromatous leprosy patients. These lepromatous leprosy patients undergo long term treatment with multi drug therapy. Among them around 73 lepromatous leprosy patients were screened for tuberculosis infection in which 55 male and 18 female.

### Collection of sputum specimens among lepromatous leprosy patients

Morning sputum specimens were collected for the study from 73 lepromatous leprosy patients in wide necked and leak proof container. Then the containers were labelled with the date, name of the patients with serial number and immediately taken to the laboratory for the analysis. Morning sputum specimens were collected from the same lepromatous leprosy patients for three continuous days.

### Transportation of sputum specimens

The collected sputum specimens were transported with the temperature of $4^0$ C to $6^0$C with coolant pack to the laboratory within two hours after collection.

### Sputum specimens analysed for *Mycobacterium tuberculosis* acid fast bacilli

The sputum specimens collected from the lepromatous leprosy patients were made over small trough glass slides as a smear. Heat fixing was done by gentle heating the slide flooded with carbol fushsin and stained for 5 min. The slide was then washed in distilled water until the excess stain is completely removed. The slide was washed with a decolorizing solvent and again rinsed in distilled water; slides were then flooded with methylene blue counter stain for 20 seconds and rinsed with distilled water. The counter stain slides were observed under oil immersion in a light microscope for acid fast bacilli.

### Microscopic examination of oral pathogens

The oral pathogens were identified from the sputum specimens by direct microscopic examination. Pus cells, epithelial cells and mucous thread were also screened and recorded.

### Knowledge, attitude, awareness and practise (KAAP) study

An extensive (KAAP) study was conducted by structured questionnaire to know about personal hygiene, practise, habit, treatment and symptoms towards the tuberculosis infection among the lepromatous leprosy patients.

## RESULTS

There has been sporadic report of co-existence of tuberculosis and leprosy in same patients. Chaussinand was the first to observe and to propose that tuberculosis could have played a major role in the disappearance of leprosy from Western Europe.

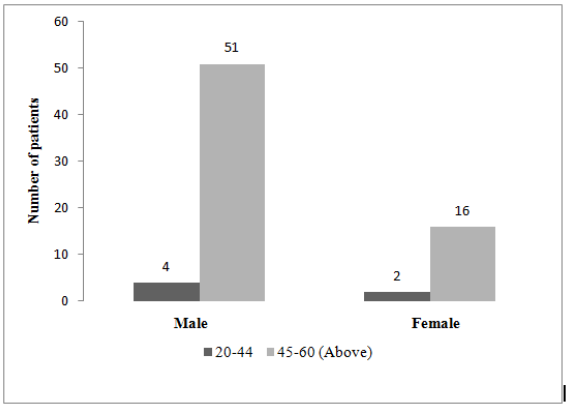


**Fig. 1. Age and sex wise prevalence of 73 lepromatous leprosy cases**

**Table 1. Sputum specimens screened for *M. tuberculosis* (AFB) smear, oral pathogens, epithelial cells and pus cells among the lepromatous leprosy patients**

| | | | Sputum for AFB | | | | | |
|---|---|---|---|---|---|---|---|---|
| **S No** | **Sex** | **Age** | **Day 1** | **Day 2** | **Day 3** | **Oral pathogens isolated** | **Pus cells** | **Epithelial cells** |
| 1 | M | 65 | - | - | - | *Bacillus sp* | - | - |
| 2 | F | 50 | - | - | - | *Streptococcus sp* | - | - |
| 3 | M | 63 | - | - | - | - | - | - |
| 4 | F | 70 | - | - | - | - | - | - |
| 5 | M | 63 | - | - | - | - | - | - |
| 6 | F | 60 | - | - | - | - | - | - |
| 7 | M | 59 | - | - | - | *Streptococcus sp, Staphylococcus sp* | + | - |
| 8 | M | 70 | - | - | - | - | + | - |
| 9 | M | 77 | - | - | - | *Staphylococcus sp, Bacillus sp* | - | - |
| 10 | F | 60 | - | - | - | - | + | + |
| 11 | M | 56 | - | - | - | *Bacillus sp* | - | - |
| 12 | F | 50 | - | - | - | - | + | - |
| 13 | F | 65 | - | - | - | *Bacillus sp* | - | - |
| 14 | M | 77 | - | - | - | - | - | - |
| 15 | M | 71 | - | - | - | - | - | - |
| 16 | M | 69 | - | - | - | - | - | - |
| 17 | M | 60 | - | - | - | *Bacillus sp* | + | - |
| 18 | M | 48 | - | - | - | *Bacillus sp* | + | - |
| 19 | M | 20 | - | - | - | - | - | - |
| 20 | M | 60 | - | - | - | - | - | - |
| 21 | M | 59 | - | - | - | *Bacillus sp* | + | - |
| 22 | M | 59 | - | - | - | - | - | - |
| 23 | F | 66 | - | - | - | *Streptococcus sp, Staphylococcus sp* | - | - |
| 24 | M | 65 | - | - | - | *Streptococcus sp, Staphylococcus sp* | + | - |
| 25 | M | 70 | - | - | - | - | - | - |
| 26 | M | 55 | - | - | - | - | - | - |
| 27 | F | 65 | - | - | - | *Staphylococcus sp* | - | - |
| 28 | F | 40 | - | - | - | - | - | - |
| 29 | F | 60 | - | - | - | *Bacillus sp* | - | - |
| 30 | F | 50 | - | - | - | - | - | - |
| 31 | F | 55 | - | - | - | *Bacillus sp* | - | - |
| 32 | M | 50 | - | - | - | - | - | - |
| 33 | M | 65 | - | - | - | *Streptococcus sp, Bacillus sp* | - | - |
| 34 | M | 64 | - | - | - | *Staphylococcus sp* | - | - |
| 35 | M | 30 | - | - | - | - | + | - |
| 36 | M | 60 | - | - | - | *Staphylococcus sp* | - | - |
| 37 | M | 55 | - | - | - | - | - | - |
| 38 | M | 68 | - | - | - | - | - | - |
| 39 | M | 58 | - | - | - | *Bacillus sp* | - | - |
| 40 | M | 45 | - | - | - | *Streptococcus sp* | + | + |
| 41 | M | 60 | - | - | - | *Bacillus sp* | + | - |
| 42 | M | 80 | - | - | - | *Staphylococcus sp* | - | - |
| 43 | M | 72 | - | - | - | *Bacillus sp* | - | - |
| 44 | M | 75 | - | - | - | *Bacillus sp* | - | - |
| 45 | M | 70 | - | - | - | *Staphylococcus s;, Streptococcus sp* | - | - |
| 46 | M | 70 | - | - | - | *Streptococcus sp* | - | - |
| 47 | M | 45 | - | - | - | *Staphylococcus sp* | - | - |
| 48 | M | 45 | - | - | - | - | - | - |
| 49 | F | 47 | - | - | - | *Staphylococcus sp, Streptococcus sp* | - | - |
| 50 | M | 40 | - | - | - | *Bacillus sp* | - | - |
| 51 | M | 57 | - | - | - | *Staphylococcus sp, Streptococcus sp* | + | + |
| 52 | M | 45 | - | - | - | *Staphylococcus sp, Streptococcus sp* | + | - |
| 53 | M | 60 | - | - | - | - | - | - |
| 54 | F | 46 | - | - | - | *Streptococcus sp, Bacillus sp* | - | - |
| 55 | M | 56 | - | - | - | *Staphylococcus sp, Streptococcus sp* | - | - |
| 56 | M | 65 | - | - | - | *Bacillus sp* | - | - |
| 57 | M | 67 | - | - | - | *Diplococci sp* | - | - |
| 58 | M | 55 | - | - | - | *Streptococcus sp* | | - |
| 59 | M | 55 | - | - | - | *Staphylococcus sp, Streptococcus sp* | | - |
| 60 | M | 47 | - | - | - | *Staphylococcus sp* | | - |
| 61 | F | 84 | - | - | - | *Staphylococcus sp* | | - |
| 62 | F | 38 | - | - | - | *Staphylococcus sp* | + | - |
| 63 | M | 66 | - | - | - | - | + | + |
| 64 | M | 67 | - | - | - | *Bacillus sp* | + | - |
| 65 | M | 45 | - | - | - | - | - | + |
| 66 | M | 57 | - | - | - | - | - | - |
| 67 | M | 60 | - | - | - | *Bacillus sp* | + | - |
| 68 | F | 40 | - | - | - | - | - | - |
| 69 | M | 55 | - | - | - | *Staphylococcus sp, Bacillus sp* | - | + |
| 70 | M | 35 | - | - | - | - | - | - |
| 71 | M | 60 | - | - | - | *Staphylococcus sp* | + | - |
| 72 | M | 55 | - | - | - | - | - | - |
| 73 | F | 70 | - | - | - | *Staphylococcus sp* | - | + |

(-) Negative for acid fast bacilli, oral pathogens, pus cells and epithelial cells in sputum specimen of lepromatous leprosy patients
(+) Presence of cells in sputum specimens of lepromatous leprosy patients

A study from literature reveals that there is an increased incidence of pulmonary tuberculosis among leprosy patients but not vice versa in South Africa (Gatner *et al.,*1980). The author reveals that individuals acquired protection against leprosy by previous infection / exposure to tuberculosis. This theory of cross-immunity between tuberculosis and leprosy lead to the hypothesis for disappearance of leprosy (Sreeramareddy *et al.,* 2007). Lepromatous leprosy patients have no or very little immune resistance to the *Mycobacterium leprae*. They are not able to mount a response because of lack of cell mediated immunity. Such infected leprosy individuals have very poor immune status and nutritional status. The lepromatous leprosy patients have severe weight loss, loss of appetite and reduction of skin fold thickness. In this context, 73 lepromatous leprosy patients were selected to screen for tuberculosis infection, living in a leprosy rehabilitation centre at Pudupatti, Madurai, Tamil Nadu, South India. Sex wise percentage of lepromatous leprosy patients taken for the study reveals that sex and age factor have direct role in the occurrence of infection. About 51% of male and 10% of female lepromatous leprosy patients were between the age group of 45 years to 60 years and above. Age and sex wise prevalence of lepromatous leprosy was presented in figure I. With regards to the practices of lepromatous leprosy patients, they were not strictly follower of personal hygiene. The sputum specimens collected from 73 lepromatous leprosy patients were screened for acid fast bacilli smear (*M. tuberculosis*) and all specimens were absent for acid fast bacilli as show in table I. This showed that there were no incidences of co-infection of tuberculosis among the selected lepromatous leprosy patients.

The sputum specimens were subjected to microscopic examination, which showed more pus cells and epithelial cells table I that confirmes that the patients were suffering from several respiratory tract infections. The biodiversity of the oral pathogens indicated that the selected individuals showed that they had acute oral infection. The occurrence of oral pathogens from selected population showed that *Staphylococcus sp* were predominantly observed in the sputum specimens followed by *Streptococcus sp*, *Bacillus sp* and *Diplococci (S. pneumoniae).* The knowledge, attitude, awareness and practices (KAAP) study of lepromatous leprosy patients reveals that they have lack of knowledge about predisposing factors for the development of leprosy and tuberculosis infection. They were illiterate and there is no awareness with reference to hygiene habits. Most of them have symptoms for respiratory tract infection such as (58%) of the patients have chest pain, (54%) have prolong cough, (22%) have cough with blood, (18%) of them develops fever and (48%) have difficulties in breathing.

## DISCUSSION

Leprosy and tuberculosis are caused by *M. leprae* and *M. tuberculosis* respectively. They are considered chronic pathogens causing diseases that take month's sometime years to develop and without treatment eventually result in a slow and painful death. Two of the oldest recognized pathogens *M. leprae* and *M. tuberculosis* have been plaguing mankind since the first stage of domestication at 10.000 years ago. Lepromatous leprosy is found in those patients with no or very little immune resistance to the *M. leprae* organism. They are not able to mount a response because of lack in cell mediated immunity. In such cases, the very defence cell the macrophage, which is meant to destroy the bacillus through phagocytosis. But the macrophages act as a favourable environment for the bacillus which plays the role of host enabling the bacillus to multiple within the cell. It has been known for up 300 *M. leprae* to fit in to one macrophage which is meant to contain the spread of the disease by ingesting and digesting such foreign organisms become a convenient vehicle for the *M. leprae* to be transported in the blood stream to all parts of the body (Rees *et al.,* 1961). In a study on a Toll Like receptor 2 (TLR2) polymorphism that was associated with lepromatous leprosy reveals that TLR2 plan an essential role in the innate immune response to *M. leprae* and that an hTLR2 polymorphism (Arg $^{677}$ Trp) was associated with lepromatous leprosy. TLR2 can also recognize the soluble tuberculosis factor culture filtrate of *M. tuberculosis* that can activate innate immune cells. Therefore in lepromatous leprosy patient will have innate immune response that may protect from the entry of *M. tuberculosis.* This cross immunity may protect the lepromatous leprosy patients from tuberculosis. The derived amino acid sequence of *M. tuberculosis* and *M. leprae* proteins are 80% identity that enhances the protection to tuberculosis infection among leprosy patients (Bochud *et al.,* 2008). In this study the selected population of lepromatous leprosy patients including 55 male and 18 female have not shown co-infection of tuberculosis. Acid fast bacilli smear were absent for all the sputum specimens. The prevalence of oral pathogens among lepromatous leprosy patients shows the presence of *Staphylococcus sp* (30%) as predominant followed by *Bacillus sp* (23%), *Streptococcus sp* (21%), and Diplococci- *S. pneumoniae* (1%). The dominant of *Staphylococcus sp* in the sputum specimens of lepromatous leprosy patients reveals that they were suffering from respiratory tract infections such as sinusitis, pneumonia, tonsillitis, and pharyngitis. In conclusion the present study of tuberculosis among the lepromatous leprosy patients indicates that the number of incidences of co-infection of tuberculosis is very less and most of the lepromatous leprosy patients were well protected from tuberculosis infection by cross immunity. Molecular analysis by extracting bacterial DNA and PCR has to be performed using primer specific for *M. tuberculosis* and *M. leprae*. PCR can be used for rapid differentiation of *M. tuberculosis* and *M. leprae* present in sputum specimen and PCR is necessary in order to screen the co-infection of tuberculosis among lepromatous leprosy patients where the occurrence of co-infection of tuberculosis is very low and the immune mechanism behind such association of both Mycobacterium diseases in a single individual can be studied and prevented.

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**Declaration of interest**

The authors report no declarations of interest. The authors alone are responsible for the content of this manuscript.

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