Research Article

Pulmonary dysfunction-an overt leprosy sequel: study done in a rehabilitation centre

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ABSTRACT

Background: In India, a total of 1.35 Lakh new cases were detected during the year 2012-13, which gives annual new case detection rate (ANCDR) of 10.78 per 100,000 populations. The proportion of multibacillary cases is 49.92%. New cases continue to occur in almost all the endemic countries indicating that high burden pocket can exist against a low burden back ground. Leprosy is a mono neuritis multiplex complex of immunological origin that results in autonomic, sensory and motor neuropathy. This impairs pulmonary chemosensitivity because of the block of vagus and sympathetic plexus in leprosy patients. Even after the treatment, a predisposition to nerve damage continues, as the clearance of bacterial antigens is extremely slow. The study aims at assessing the respiratory function in treated leprosy patients.

Methods: 23 treated leprosy patients were selected after written and informed consent according to the inclusion and exclusion criteria. After obtaining the clearance from Institutional ethical committee, pulmonary function test was performed and the lung parameters were measured using computerized spirometry.

Results: The statistical analysis revealed significant decrease in FVC%, FEV1%, FEV1/FVC% in lepromatous patients compared with tuberculoid patients. The restrictive pattern predominates in both lepromatous and tuberculoid patients.

Conclusions: The study concluded that there is a definite impairment of lung functions in the patients treated for leprosy, causing spontaneous respiratory arrest and unexplained sudden deaths. Since the results have statistical significance, the study warrants early detection of respiratory abnormalities in leprosy patients who don’t have any clinically detectable symptoms.

Keywords: Pulmonary function test functions, Leprosy-treated patients, Respiratory impairment, FVC%-restrictive pattern

INTRODUCTION

The WHO expert committee on leprosy, eighth report, defined a case of Leprosy as a person having manifestations of at least one of the following cardinal signs.

Definite loss of sensation in a pale (hypo pigmented) or reddish skin patch. A thickened or enlarged peripheral nerve, with loss of sensation and/or weakness of the muscles supplied by the nerve. The presence of acid-fast bacilli in a slit skin smear.

Epidemiology

Worldwide, 2 to 3 million people are estimated to be permanently disabled due to leprosy.
New leprosy cases reported by 115 countries in 2012 were 232857 among which 166445 cases were from South East Asia especially 134752 cases from India. India is one among the 16 countries reporting more than 1000 new cases annually since 2005. A total of 1.35 Lakh new cases were detected during the year 2012-13, which gives Annual New Case detection rate (ANCNR) of 10.78 per 100,000 populations. This shows increase in ANCDR of 4.15% from 2011-12. The proportion of Multi bacillary cases is 49.92% as highlighted in NLEP progress report. New cases continue to occur in almost all the endemic countries indicating that high burden back ground states WHO in Global leprosy situation.

**Classification**

Leprosy is a classical spectral disease manifesting in a variety of clinical forms related to the type and strength of the immune response.

If the Cell Mediated Immunity (CMI) is deficient, the disease spreads uncontrolled and produces Multi bacillary Leprosy with multi system involvement. Specific cell mediated immunity if effective, it eliminates or controls the infection in the body, by which the lesions heal spontaneously and it produces paucibacillary type of Leprosy.

In 1981, the WHO study group on chemotherapy of Leprosy for control programs classified leprosy as multibacillary and paucibacillary according to the degree of skin smear positivity. Multibacillary leprosy included polar lepromatous (LL), borderline lepromatous (BL) and mid Borderline (BB) cases in the Ridley-Jopling classification. Paucibacillary leprosy included indeterminate (I), polar tuberculoid (TT) and borderline tuberculoid (BT) -WHO Expert Committee 8th report.

**Clinical spectrum of leprosy**

At one end of the clinical spectrum is tuberculoid leprosy, characterized by sparse skin lesions with few bacilli adding on to the development and recruitment of T lymphocytes that contribute to the control of infection. At the other extreme is lepromatous leprosy characterized by a large number of skin lesions with abundant bacilli, clinically apparent infiltration of peripheral nerves with the presence of fewer T lymphocytes in lesions whose effector mechanisms are unable to control the infection. In the absence of treatment, Paucibacillary form may downgrade to Multi bacillary form through borderline spectrum.

Nerve involvement in leprosy is much more serious and causes progressive disability and crippling deformities because neurons if destroyed do not regenerate and are replaced by fibrous tissue. Leprosy causes a mononeuritis multiplex of immunological origin that result in autonomic, sensory and motor neuropathy. Among all the components of peripheral nervous system, the impact of autonomic dysfunction is noteworthy in leprosy. The peripheral autonomic fibers are commonly involved especially the sensory fibers which are affected early in leprosy, as shown by the characteristic dryness, roughness of the skin and anhydrosis.

There is impairment of pulmonary chemo sensitivity because of the block of vagus and sympathetic plexus in leprosy patients as explained by Gupta OP. The morphological involvement of sympathetic chain and vagus nerve in leprosy substantiate the definite involvement of autonomic neuropathy.

Anti-Leprosy treatment on its own has no beneficial effect on leprosy reactions or leprosy neuropathy and there is development of new neurological or cutaneous symptoms in patients released from Leprosy treatment after a variable range of time. So, even after the treatment, a predisposition to nerve damage continues, as the clearance of bacterial antigens is extremely slow.

**Neuropathy in leprosy**

Leprosy, a chronic granulomatous disease caused by Mycobacterium leprae, principally affecting skin and peripheral nerves, implicating both somatic and autonomic nerve fibers.

Leprosy is one of the leading causes of severe neuropathy in the tropics and the subtropics and also the commonest peripheral neuropathy in the world as stated by Darab K. Dastur causing morbidity and permanent severe disability due to sensory loss and motor paralysis which remains the prime focus of clinical consent and research. Apart from sensory loss and motor paralysis, autonomic neuropathy is reported in varying degrees as indicated by sweat function test, histamine triple response and bed side tests for cardiovascular and respiratory system involvement in Leprosy.

Autonomic dysfunction in leprosy was reported earlier by Arnold, from loss of sweating in patches and also by Mathur and Pasricha from reduced sweat response and vasodilatory effect. Mathur et al also said the degree of impairment of autonomic functions did not always correlate with the loss of sensations. Long standing lepromatous leprosy have definite autonomic involvement demonstrated by kyriakidis, et al concluding definite impairment of both parasympathetic and sympathetic control of cardiovascular autonomic integrity.

The inflammatory infiltration and the presence of lepra bacilli in the ganglion cells of sympathetic ganglion in lepromatous patients has been demonstrated by Ermakova and Lumsden has also shown the involvement...
of sympathetic nerve involvement in histological studies. Crawford et al documented no visceral autonomic neuropathy in 20 leprosy patients. Desikan K.V et al studied that the lung parenchyma and central nervous system are not affected by Leprosy.19,20

**Bacillemia**

S. Kaur et al while discussing on the occurrence of bacillemia substantiated the lung parenchymal involvement by documenting infiltration in right apical upper and mid zones. Carlos A.M Silva et al 2013, showed that Mycobacterium leprae, the causative agent of leprosy can enter human alveolar and nasal epithelial cells and both cell types are capable of sustaining bacterial survival and the delivery of Mycobacterium leprae to nasal septum resulted in macrophage and epithelial cell infection in lungs tissue in their studies.21,22

The pulmonary parasympathetic inflammatory reflex which functions as a requisite regulator for lung infection, inflammation and immunity as studied by X.Yang et al23, 2014 was impaired in leprosy patients shown by impaired cough reflex and prolongation of breath holding time as demonstrated by Malik et al.24,25 33% abnormal Valsalva score and 66.7% abnormality in single deep breathing was demonstrated by Neelan et al.26

Aim of the study was to evaluate lungs functions in treated leprosy patients using spirometry, to assess the respiratory and cardiovascular parameters clinically, to evaluate Lung functions using computerized spirometry and determine the proportional impact and to Compare the lung parameters among lepromatous and tuberculoid patients.

**METHODS**

It was a cross sectional study. Duration of the study was 2 months (3 July to 4 September).

Place of the study Spiro lab. 23 treated Leprosy cases selected according to the inclusion and exclusion criteria.

**Inclusion criteria**

- Treated Leprosy patients.
- Normal BMI.
- Both genders.

**Exclusion criteria**

- Subjects with respiratory illness.
- Current acute respiratory disease
- Current respiratory symptoms
- History of asthma
- Current treatment with asthma medication
- History of chronic obstructive pulmonary disease Or chronic bronchitis
- Thoracic surgeries
- Pulmonary embolism
- Smokers.
- Subjects with spinal and chest wall deformities.
- Subject with CAD
- Subjects with diabetes mellitus, hypertension and hypothyroidism.
- Alcoholics
- On medications through puff or by respiratory route

After obtaining clearance from the Institutional Ethics Committee, Permission from the Rehabilitation centre and written informed consent from each subject, the detailed procedure and purpose of the study were explained and performed.

**Equipment setup**

The procedure was based on the current standards for pulmonary function, equipment, testing, and interpretation set by the American Thoracic Society (ATS)/ERS 2005 specified spirometry standardization. The easy one PRO [1.2.0.7] (en)/ EASY ONE PRO [4.3.9.27] NDDmedizintechnikAG are the computerized pulmonary function testing equipment.

Laboratory assessments was performed in EASY ONE PRO and the generalized system of instrumentation performance was be done based on Quanjer, et al 199327, 33%

**Procedure**

The procedure to spirometry consists of deep inspiration followed by forced expiratory maneuver, maintained until the individual no longer tolerate, or until the acceptance criteria proposed by the guidelines for Pulmonary Function Tests of American thoracic society. All the subjects performed at least three forced vital capacity maneuvers. In our study, Leprosy patients were able to reach only average subjective parameters designed in standard spirometry assessment.

- Parameters Assessed
  - Forced Vital Capacity(FVC)
  - Forced Expiratory Volume at 1st second.(FEV1)
  - FEV1/FVC
  - Forced Expiratory Flow 25%-.75 % ( FE25%-.75%).
  - Peak Expiratory Flow.(PEF)
  - Forced Expiratory Time.(FET)
  - Forced Inspiratory Vital Capacity.(FIVC)
  - Peak Inspiratory Flow.(PIF)
The predicted values were obtained from the reference values for adults reported by American Thoracic Society and spirometric settings. The Spirometric parameters were displayed and all data with flow-volume and volume time curves were documented.

RESULTS

The sample consisted of 23 subjects of which 12 were lepromatous and 11 were tuberculoid of the age group 45-80. The data obtained showed a mean age of 63.8±10.0 and BMI of 20.5±1.4 which were not statistically significant that rules out the influence of confounding variables (Table 1).

Of the 23 patients evaluated, the mean duration of treatment of Lepromatous patients was 8.17±2.2 and had lepra reactions during the course of treatment. The study had 11 tuberculoid Leprosy patients with mean duration of treatment of 4.00±3.09 with uneventful course of treatment (Figure 1). On comparison, the duration of treatment was statistically significant between the two groups.

Based on the physical examination, they didn’t have any acute or chronic respiratory problems. The impairment in the lung were assessed using the GOLD® standard values of FVC%, FEV1% and FEV1/FVC % (*spirometry for health care providers, Global initiative for chronic obstructive pulmonary disease GOLD). The mean Forced Vital Capacity percentage for lepromatous patients is 51.75±15.2 and that of tuberculoid patients is 84.63±11. This shows that lepromatous patients have significantly lower FVC% when compared with tuberculoid patients. (Figure 2).

The mean forced expiratory volume at first second percentage for lepromatous patients is 55.08±10.91 and that of tuberculoid patients is 91.27±13.71. This shows that lepromatous patients have significantly lower FEV1% when compared with tuberculoid patients. (Figure 3).

Out of the 23 patients evaluated, 7 (30.4%) had normal pulmonary function parameters, 16 (69.6%) had impaired pulmonary function parameters. Significantly, subjects with Lepromatous Leprosy (75%) had definite impaired pulmonary function than tuberculoid (25%) (Table 2). In the comparison between respiratory dysfunction and the type of leprosy, restrictive pattern seem to be predominate in both Lepromatous (66.7%) and tuberculoid patients (Figure 4).
tuberculoid (36.4%). There were no obstructive cases in tuberculoid type (0%) and 4 Lepromatous patients showed obstructive pattern (33.3%) (Table 3).

The mean ratio of forced expiratory volume at first second to forced vital capacity percentage for lepromatous patients is 93±12.69 and that of tuberculoid patients is 111.22±13.31. This shows that lepromatous patients have significantly lower FEV1/FVC% when compared with tuberculoid patients. Fig 4; Reduction in both FEV1 and FVC in treated Lepromatous patients has not caused significant change in FEV1/FVC% suggesting Restrictive pattern.

The data obtained showed in (Table 1) a mean age of 63.8±10.0 and BMI of 20.5±1.4 which were not statistically significant that rules out the influence of confounding variables. Age and BMI were not statistically significant.

**Table 1: Age and BMI.**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Type of leprosy</th>
<th>Number of patients</th>
<th>Mean ± standard deviation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Lepromatous</td>
<td>12</td>
<td>63.25±10.8</td>
<td>0.78</td>
</tr>
<tr>
<td>Tuberculoid</td>
<td>11</td>
<td>64.45±9.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>Lepromatous</td>
<td>12</td>
<td>1.99±1.3</td>
<td>0.06</td>
</tr>
<tr>
<td>Tuberculoid</td>
<td>11</td>
<td>2.1±1.4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table 2: Lung functions.**

<table>
<thead>
<tr>
<th>Patients</th>
<th>Lung functions</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Impaired</td>
</tr>
<tr>
<td>Number</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Proportion</td>
<td>30.4%</td>
<td>69.6%</td>
</tr>
</tbody>
</table>

Significantly, subjects with lepromatous leprosy (75%) had definite impaired pulmonary function than tuberculoid (25%). Nearly 70% of the treated leprosy patients showed definite pulmonary dysfunction.

**Table 3: Obstructive and restrictive.**

<table>
<thead>
<tr>
<th>Type of leprosy</th>
<th>Lung functions</th>
<th>Total</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>Obstructive</td>
<td>Restrictive</td>
</tr>
<tr>
<td>Lepromatous</td>
<td>0 (0)%</td>
<td>4 (33.3)</td>
<td>8 (66.7%)</td>
</tr>
<tr>
<td>Tuberculoid</td>
<td>7 (63.6%)</td>
<td>0 (0%)</td>
<td>4 (36.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>7</td>
<td>4</td>
<td>12</td>
</tr>
</tbody>
</table>

In (Table 3) the correlation between respiratory dysfunction and the type of leprosy, restrictive pattern seem to be predominate in both Lepromatous (66.7%) and tuberculoid (36.4%). There were no obstructive cases in tuberculoid type (0%) and 4 Lepromatous patients showed obstructive pattern (33.3%).

**DISCUSSION**

The study was focused to find out the pulmonary dysfunction in 23 patients treated for leprosy of which 12 were lepromatous and 11 were tuberculoid, who had completed their treatment with the mean period of 28.17 years at the time of enrollment of the study.

In our study the mean duration of treatment of lepromatous patients were 8.17±2.21 and for the tuberculoid it was only 4.0±3.1, supporting the fact of effective cell mediated immunity in tuberculoid leprosy. The Lepra reactions which increased the duration of treatment are initiated by the release of mycobacterial antigens that leads to the formation of immune complexes and complement activation. This complicates leprosy with the involvement of multiple organ systems. Even in our study of the 12 lepromatous patients, 8 had lepra reactions which prolonged the treatment and the pulmonary function tests was also found to be significant.

In all forms of leprosy, Lumsden states there occurs the presence of bacilli housed in the Schwann cells. The heavy infiltration of lepra bacilli in the dorsal root ganglion, sympathetic chain and the vagus emphasized the centripetal involvement of nervous system in the lepromatous leprosy. Also the lepra bacilli were found in the bronchial smears and the alveolar epithelial cells in a study done by S. Kaur et al. The pulmonary
The neural damage in leprosy related to the respiratory system was indicted by reduction the respiratory muscle strength and the reduction may be due to the chronicity of the disease in which the affected individual have the disease sequelae and high levels of physical disability. Forced vital capacity measure the change in lung position from maximal inspiration to maximal expiration considered a measure of the subject’s ability to change the size of the thoracic cavity. This is influenced by all the muscles of respiration with their innervations, by lung elasticity and by the patency of the airways.

On the contrary, Laul Negrao Bleury et al suggested, obstructive pattern of airway disease is less documented in Leprosy highlighting the fact that unless and until the leprosy patients have laryngeal involvement causing acute emergencies, obstructive airway disease is rarely encountered. Restrictive pattern, which is predominating in this study correlates well with the earlier findings substantiating the underlying neuromuscular dysfunction.

Hence focus has to be made on the implementation of rehabilitation protocols for lungs in patients with sequelae of leprosy and public health policies that focuses on primary, secondary and tertiary care in this population.

**CONCLUSION**

The study concluded that there is a definite impairment of lung functions in the patients treated for leprosy, both lepromatous and tuberculoid type as evidenced by a decrease in FVC% and FEV1% which was statistically significant.

In this sample, all the lepromatous patients showed significant pulmonary dysfunction consistent with their increased duration of treatment due to lepra reactions contributing to the respiratory dysfunction. Due to effective Cell Mediated Immunity (CMI) tuberculoid patients had minimal respiratory dysfunction as revealed by our study that only 4 out of 11 had respiratory decomposition. In this study restrictive pattern of lung dysfunction seems to predominate. The reason could be underlying respiratory muscle weakness as evidenced by earlier studies like impaired cough reflex and prolonged breath holding time. Since the results have statistical significance, the study warrants early detection of respiratory abnormalities in leprosy patients who don’t have any clinically detectable symptoms.

With the precise transmission mechanism of leprosy still unknown and a lack of an effective vaccine, leprosy will probably continue to pose an ongoing public health problem in the coming decades.

The goal of WHO is to reduce the rate of new cases with grade 2 disabilities worldwide by at least 35% by the end of 2015. So, the add on screening for co-morbid condition could subdue the debilitating sequelae of the disease. Increased empowerment of the people affected by the disease together with their greater involvement in services and community will bring us to a world without leprosy.

**Summary**

The study aimed to investigate the pulmonary function test in patients treated for leprosy and their correlation with type of leprosy and duration of treatment of the disease. In this sample, individuals treated for leprosy showed restrictive pattern of lung dysfunctions predominantly.

The results showed a positive and statistically significant correlation between the lepromatous leprosy and the lung impairment. Longer the duration of treatment higher is the lung impairment.

Approximately 2 to 3 million individuals with leprosy have some degree of physical impairment and about 20% present with physical disabilities and psychosocial constraints even after treatment.

Some kind of intervention in rehabilitation like breathing exercises, respiratory muscle endurance training related activities can be included as a part of continuing medical care to improve their quality of life and reduce the morbidity.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** The study was approved by the Institutional Ethics Committee

**REFERENCES**

1. WHO Expert Committee on leprosy: eighth report. (WHO technical report series; no. 968)