# Ocular Manifestations of Leprosy Patients on Multidrug Therapy in a Teaching Hospital of South Karnataka

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**ABSTRACT**

**BACKGROUND**

Leprosy is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*. Several ocular manifestations occur before and during multi drug therapy (MDT) and they can continue to occur even after the completion in bacteriologically cured patients. Blindness is a catastrophic event that can occur by several mechanisms at any stage. We need to learn and recognise the early signs and symptoms of ocular complications, so that we can treat the patient early. We need to evaluate the pattern of ocular manifestation in leprosy patients on MDT (Multi Drug Therapy).

**METHODS**

A cross-sectional study was conducted over a duration of six months on diagnosed cases of leprosy and those cured from leprosy. Data was collected by clinical history with slit lamp examination, fundus examination, and laboratory investigation.

**RESULTS**

Total 30 patients were included in the study in which 13 patients were on MDT, 7 newly detected cases and 10 treated cases. 22 were males and 8 were females with male - female ratio of 2.75:1. Average age of presentation was 46 years with range from 18 - 80 years. 56 % had ocular manifestations in this study. Ocular lesions were more in cases who had leprosy for ≥ 16 years. Visual acuity ranged from 6 / 6 to PL + ve. Lagophthalmos was noted in 4 cases, cataract in 6 cases, exposure keratitis in 2, chalky white deposits on cornea in 2, spheroidal degeneration in 2, iris atrophy in 2, and pterygium in 2 cases.

**CONCLUSIONS**

Patients who completed treatment for MDT require periodic monitoring to detect ocular morbidity early and to prevent visual loss.

**KEYWORDS**

Leprosy, Multidrug Therapy, Exposure Keratitis, Lagophthalmos

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## BACKGROUND

Leprosy word is derived from the French word "leper" and from the Greek word "lepros" which means scaly, referring to the scales that form on the skin. The most ancient writings of ‘‘SUSHRUTA SAMHITA’’ compiled in 600 BC refers to leprosy as Vata Rakta or Vat Shonita and Kushtha. Leprosy occurs in all ages and both sexes.[1]

First scientific study on leprosy was conducted by Norwegian researcher Daniel Cornelius Danielssen (1815 - 1894) and Carl-Wilhelm Boeck (1808 - 1875).[2] Gerhard Armauer Hansen described leprosy was not hereditary but contagious disease with lepra bacillus discovered in 1873.[2]

In the world according to WHO, 16 million leprosy cases have been cured over the last 20 years. Prevalence rate of leprosy has dropped to 0.25 per 10,000 in 2017 from 21.1 cases per 10,000 populations in 1985. In 2017 new case detection rate was 2.77 / 100,000 population. In 2017 total new cases of about 210, 671 were detected. 73 % of the global burden encountered in SEAR (South East Asia Region) and in that India and Indonesia contributed about 67.4 % of the new leprosy cases globally and 92.6 % regionally.[3]

Leprosy, is a chronic granulomatous infectious disease caused by *Mycobacterium leprae*.[3] It is straight / slightly curved, rod shaped, intra cellular acid-fast bacilli and grows slowly. It looks like agglomerates, being bound by a lipid substance 'glia'. These masses are known as 'GLOBI'. Parallel rows of bacilli in globi gives 'cigar bundle' appearance. It primarily affects the peripheral nerves and skin but also can involve other tissues like eyes, mucosa of the upper respiratory tract, muscles, bones, the reticuloendothelial system and testes.[4] Its transmission from person to person occurs through infected respiratory droplets and can infect others by entering through breaks in the skin but cannot infect intact skin. The upper respiratory tract appears the most likely portal of entry.

Systemic disease manifests in two ways - Lepromatous leprosy and Tuberculoid leprosy. Lepromatous leprosy is a multisystemic infection and its manifestation includes leonine facies (Characterised by cutaneous thickening, nasal widening and thickening of ear lobules), saddle shaped nasal deformity, peripheral nodules and cutaneous plaques, Claw hands, shortening and loss of digits. In Tuberculoid Leprosy it is restricted to the skin and peripheral nerves such as annular anaesthesia, hypo pigmented skin lesions and thickening of peripheral nerves. In lepromatous form with decreased cell mediated immunity, direct ocular involvement will be there and iris pearls have Macrophages filled with bacilli. In Tuberculoid Leprosy, patients will have good Cell Mediated Immunity and indirect ocular involvement such as neurotrophic and neuroparalytic keratopathy. Tuberculoid form will have granuloma formation and lack of large number of bacilli because of good cell-mediated immunity. Systemic manifestations in skin include Hypopigmentation, Erythema nodosum, plaques and nodules. Nerve involvement will cause skin anaesthesia, thickened peripheral nerves and facial palsy. Deformities noted in leprosy includes Saddle shaped nose, leonine facies and claw hand (ulnar nerve palsy). Lepromatous leprosy is a common cause of eye complications.

WHO classified leprosy into Indeterminate Leprosy, Tuberculoid Leprosy, Borderline Tuberculoid Leprosy, Mid - borderline leprosy, Borderline Lepromatous leprosy and Lepromatous Leprsosy.

Leprosy remains one of the world's blinding disease. Blind leprosy patients have irreversible double tragedy. They can neither see nor feel causing great burden on themselves as well as the relatives. In eyes, extra ocular structures and anterior segments are commonly affected.

For treatment purposes, Leprosy is grouped into 2 categories: Multibacillary and Paucibacillary.[5] Ocular involvements in leprosy is especially high in the Multibacillary type of leprosy.[6] Blindness in leprosy is caused by lagophthalmos, uveitis, corneal hypoesthesia, secondary glaucoma, and cataract. Other ocular manifestations noted are conjunctivitis, hypopigmented nodules, Tarsal plate thickening leading to mechanical ptosis, thickening of corneal nerves, decreased corneal sensations, neuroparalytic keratitis, corneal pannus. In uvea it causes acute iritis due to immune complex deposit and chronic iritis due to direct invasion. In granulomatous uveitis there will be formation of mutton fat large keratic precipitates, patchy dense synechia, low grade flare, nodules over iris, hypopigmented patches over the iris, complicated cataract, secondary vitreous degeneration, retinal pearls, choroidal thickening, choroidal detachment. Optic nerve involvement is rarely seen. In leprosy, cranial nerve most commonly involved is VII and other cranial nerves involved in decreasing order are V, VI, IV and III. The reported prevalence of blindness varies from 0.7 % and 30 %.[7]

Cornea is supplied by anterior ciliary nerves which are branches of ophthalmic division of the 5th cranial nerve. Lepromatous infiltration causes nerve thickening, causing corneal anaesthesia. Lepromatous infiltration of 7th cranial nerve especially the zygomatic branch causing paralysis of the orbicularis oculi muscles. Patient is unable to close the eyes resulting in staring look, because of lagophthalmos failure of eyelid function leading to corneal ulceration. Because of decreased corneal sensation patients have no symptoms and eyes are neglected causing perforation of ulcer, intraocular infection and eventually blindness. Cornea is avascular structure. *M leprae* invades either from adjacent structure or along the nerves, causing micronodules. Since the cornea is transparent these nodules can be easily seen as dense white corneal pearls and causes diffuse superficial punctate keratitis.

Conjunctiva involvement occurs because of continued exposure leading to chronic conjunctivitis. Erythema nodosum leprosum lesions appear on the conjunctiva. In pterygium cases collection of macrophages containing *M. Leprae* has been reported.

Iris granulomatous lesions cause iritis and iridocyclitis. Chronic iridocyclitis may lead to formation of cataract. Steroids used in the treatment of lepra reactions may hasten the formation of sub capsular cataract. Ulceration in granulomatous lesion may produce an exudate composed of fibrin and polymorphs and the pupillary margins may adhere to the anterior capsule of the lens causing posterior synechia, resulting in fixed, narrow, non reacting pupil. Eventually, destruction of the tissue of the iris and ciliary

body causes atrophy and shrinkage of the globe known as phthisis bulbi. Iris Pearls occur because of collection of lepra bacilli and they adhere to pupillary margins and iris surface like necklace and the pearls will enlarge slowly and coalesce gradually leading to peduncle formation and that will drop in anterior chamber and disappear leading to iris atrophy and meiosis.

Scleritis is seen in long term untreated cases and it may produce nodules at sclero-corneal junction and may weaken the globe. Episcleritis is rarely seen. Posterior segment involvement is very rarely noted in leprosy. These are extension of lesions from ciliary body to the choroid and retina manifesting as yellowish nodules. Investigation for leprosy includes skin biopsy, skin Test-Lepromin test (Mitsuda reaction). For culture specimen collected from skin, ear lobules, nasal mucosa and smear stained with Ziehl-Neelsen stain using 5 % H2SO4 acid for decolourization.

Lepra reaction is acute or subacute inflammation mediated by immunological reaction. It is usually diagnosed by clinical examination. Inflammatory changes in skin lesions or appearance of new lesions, patches or nodules with acute onset. Two types of reactions occur - Reversal reaction (type1) and Erythema Nodosum Leprosum (ENL or Type 2). Both types of reaction can occur at the start of MDT, during course or after completion. In severe ENL reaction, pain occurs in the eye with or without redness of eye and sometimes there will be loss of visual acuity.[8]

Leprosy is endemic in India with the prevalence of 3.8 per 10000 persons.[9] At the start of 2005, 70 % of the world's registered leprosy patients lived in India.[10]

Ocular manifestations may derive not only from the disease per se, but also due to reactions to drug therapy.[11,12] Although patients who have completed treatment are considered cured (because most of them are microbiologically negative) they still have many disabilities which were present before treatment began. In addition, they may have progressive disability because of pre-existing nerve damage which is not reversed by treatment. Thus, it is possible that after leprosy cure, new ocular pathology may develop.[12,13]

LROP (Leprosy Related Ocular Pathology) was defined as the presence of one or more of the following features such as: lagophthalmos, corneal nerve beading, punctate keratitis, corneal opacity and presence of uveal involvement (cells and flare, iris atrophy and/or keratic precipitate). PBLROP (Potentially Blinding Leprosy Related Ocular Pathology) was defined as leprosy related conditions leading to visual loss due to uveal involvement and / or lagophthalmos.[13]

In the epidemiology of leprosy cases there is gradual shift in type of leprosy patients from paucibacillary to the multibacillary forms and also there is increase in case detection rate in older age group compared to younger age group. By improving socioeconomic status and health care facilities there will be increase in survival.[14] There was consensus that the prevalence of ocular complications can be reduced with the introduction of ophthalmic examination from diagnosis and to continue evaluation even after completion of multidrug therapy. There is currently little information about the magnitude and nature of incidence of ocular pathology in patients on MDT.

### Objectives

1. To report the prevalence of ocular morbidity in leprosy patients.
2. To determine ocular manifestations of leprosy patients on MDT and those cured from leprosy.
3. To evaluate the visual acuity in leprosy patients on MDT.

## METHODS

This hospital based observational cross-sectional study was conducted at Mandya Institute of Medical sciences from October 2018 to March 2019 in accordance with tenets of the Declaration of Helsinki. Ethical clearance was obtained from Institutional Ethical committee with IEC No. MIMS / IEC / RP / 2018 / 235. Study duration was 6 months with sample size of 30 taken using purposive sampling method. 30 patients, with leprosy registered for the MDT and cured from leprosy, visiting Ophthalmology OPD with ocular complaints were included in the study and also both Paucibacillary and Multibacillary leprosy cases were included in the study.

All Patients with age less than 18 years and those who had history of Diabetes mellitus, hypertension and ocular trauma, which could have overlapping manifestation with leprosy, were excluded from the study.

Study was started after obtaining consent from patients and witness regarding their involvement in the study. Detailed demographic profile of the patients including age, gender, occupation and duration of leprosy with brief ocular history was taken. Unaided visual acuity and Best Corrected Visual Acuity (BCVA) using Snellen's chart and for near vision using Jaegers chart, anterior segment examination by Slit lamp bio microscope. Ocular motility and posterior segment examination using indirect ophthalmoscope and 20 Dioptre lens after dilatation of pupil was conducted. Corneal sensation was checked with the help of wisp of cotton. Intraocular pressure recorded using Schiotz tonometer.

During ocular examination we mainly focused on loss of eyebrows, poliosis, trichiasis, lagophthalmos, orbicularis oculi muscle weakness, eyelid abnormalities, corneal ulcer, corneal opacity, clofazimine crystal deposition on conjunctiva and cornea, presence of episcleritis and scleritis, anterior chamber cells and flare, presence of iris atrophy, posterior synechia, pupillary reaction to light and presence of cataract.

Whenever we suspected cataract or synechia we dilated using mydriatic drops (tropicamide and phenylephrine) and examined under slit lamp. Best corrected visual acuity was measured by a trained examiner using a Snellen chart. Cases with less visual acuity and / or with intraocular complications were examined by indirect ophthalmoscope after pupillary dilation.

Slit skin smear and skin biopsy was performed by the Dermatologist and report obtained as positive for *Mycobacteria leprae* (Ziehl Neelsen technique of staining)

Patients with eye manifestations were treated according to their need such as Lubricant drops, topical antibiotic with steroid drops, antibiotic eye ointments, physiotherapy, frequent blinking exercises and lid taping with micropore plaster at night time and spectacle correction.

### Statistical Analysis

Data was entered in Microsoft Excel and analysed using Epi-info software. The results were expressed in proportions.

## RESULTS

A total of 30 patients were studied, out of which 22 patients were males (73 %) and 8 were females (27 %) with male to female ratio of 2.75: 1. The age group of the patients ranged from 18 to 80 years, with a mean of 46 years. Out of 30 patients, 13 were on MDT (43.33 %), 7 (23.33 %) were newly detected cases and 10 (33.33 %) were old cases.

Two patients were below 30 years' age group, 12 patients in 30 - 39 years' age group, 6 patients in 40 - 49 years' age group and 10 patients in 50-59 years' age group were present. Majority of patients were in between age group of 30 - 39 years (Table 1). Occurrence of ocular lesions due to leprosy was found to be more in patients with more than 16 years' duration of leprosy. 23 % of patients had Best corrected visual acuity (BCVA) between 6 / 18 to 6 / 36 and 20 % of patients had visual acuity below 6 / 60 and remaining had visual acuity better than 6 / 12 (Table 2).

| | Demographic Characteristics | With Ocular Manifestation N (%) | Without Ocular Manifestation N (%) |
|---|---|---|---|
| Sex | Male | 12 (75 %) | 10 (71.42 %) |
| | Female | 4 (25 %) | 4 (28.57 %) |
| | **Total** | **16 (53.33 %)** | **14 (46.66 %)** |
| Age | < 30 | 0 | 2 (14.28 %) |
| | 30 - 39 | 6 (37.5 %) | 6 (42.85 %) |
| | 40 - 49 | 4 (25 %) | 2 (14.28 %) |
| | > 50 | 6 (37.5 %) | 4 (28.57 %) |
| | **Total** | **16 (53.33 %)** | **14 (46.66 %)** |

***Table 1. Distribution of Demographic Characteristics and Ocular Manifestations of Leprosy Patients***

| Ocular Manifestations | No. of Patients N (%) |
|---|---|
| Lagophthalmos | 4 (25 %) |
| Cataract | 6 (37.5 %) |
| Pterygium | 2 (12.5 %) |
| Exposure keratitis | 2 (12.5 %) |
| Chalky white deposits on cornea | 2 (12.5 %) |
| Anterior Synechia | 2 (12.5 %) |
| Spheroidal degeneration | 2 (12.5 %) |
| Nystagmus with exotropia | 1 (6.25 %) |

***Table 2. Different Types of Ocular Manifestations in the Cases Having Ocular Involvement***

Ocular manifestation was found to be more in males (73 %) compared to females (27 %). Ocular manifestation was more in patients in age of more than 50 years (33.33 %) and also in age group of 30 - 39 years (40 %). Lagophthalmos was seen in 4 cases (25 %), cataract was seen in 6 cases (37.5 %), iris atrophy was seen in 2 cases (12.5 %), Corneal involvement was seen in 6 cases in that spheroidal degeneration was seen in 2 cases (12.5 %), exposure keratitis was seen in 2 cases (12.5 %), chalky white deposits on the cornea was seen in 2 cases (12.5 %), medullated nerve fibre was found in 1 case (6.25 %), glial tissue at optic disc was found in 1 case (6.25 %), 2 cases (12.5 %) had nasal Pterygium and one (6.25 %) case had mild ptosis. (Table 3 & 4) One case (6.25 %) had Nystagmus with Exotropia associated with Visual evoked potential (VEP) abnormality showing afferent pathway defect in right eye more than left eye.

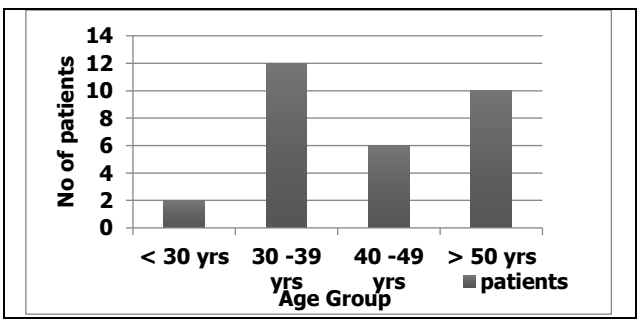


***Figure 1. Age Distribution of Leprosy Patients on MDT***

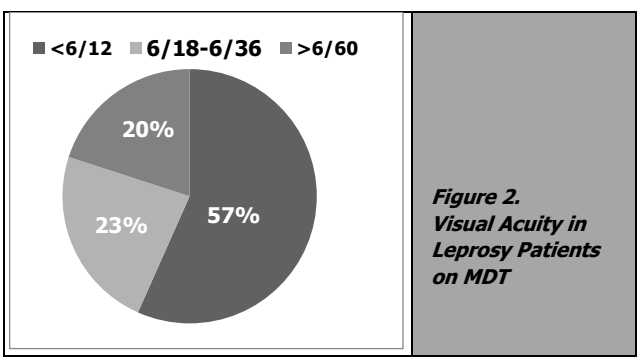


***Figure 2. Visual Acuity in Leprosy Patients on MDT***

## DISCUSSION

Many studies have been conducted to estimate prevalence of ocular manifestation in leprosy patients. Ocular manifestation depends on the duration of the disease, therapeutic intervention and duration of treatment and compliance of the patients.

Most common cause of visual impairment in our study was cataract. Leprosy cases have three times increased risk of development of cataract. In our study cataract was found in 6 patients (37.5 %), which was almost similar to study conducted by Lewallen S et al. showed 34.5 %of cases.[6] Parikh et al. showed that cataract was the most important cause of visual impairment (51 %).[10] In Daniel E et al. study it was found to be lesser of about 4 cases (6.6 %).[11] Finding of cataract depends on the method of examination such as slit examination. Cataract development depends on the age of the patients. Increased risk of development of cataract in leprosy patients is because of infiltration of iris by leprosy bacilli and it promoting cataract growth.

Lagophthalmos is the inability to close the eyelids normally. In leprosy patients it can occur before, during or after MDT treatment. Lagophthalmos along with decreased corneal sensation can lead to exposure keratitis, ulceration and opacification of cornea**.** In our study 4 patients (25 %)

had lagophthalmos which was almost similar to Lewallen S et al. study in which 18.5 % had lagophthalmos.[6] Daniel E et al. (5 %) and Parikh R et al. (10.4 %) studies showed to be lesser than present study.[10,12]

In leprosy, cornea is extremely vulnerable to injury due to reduced corneal sensations and secondary infection in exposure keratitis (lower half), resulting in opacification of cornea. In our study we found 2 patients (12.5 %) had exposure keratitis which was almost similar to Parikh R et al. study (10.4 %),[10] in other studies such as Daniel E et al. and Lewallen S et al. showed 6.6 % and 20.1 % respectively.[6,12]

In our study we noted that 2 cases (12.5 %) had chalky white deposits (Band Keratopathy) on the cornea which was present in both eyes. Most of the studies did not mention chalky white deposits and their significance.

Uveitis or iridocyclitis is an inflammation of the iris and ciliary body. It indicates that autoimmune inflammation due to para infectious mechanism. It is the most common cause of blindness in leprosy patients. Leprosy is one of the most important causes of infectious iridocyclitis. It is the favourable site for the growth of the leprosy bacilli as iris and ciliary body will be cooler than core body temperatures leading to chronic iritis. It is thought to be due to sympathetic nerve damage in leprosy, sub-clinical infections will be more. In our study iris atrophy was noted in 12.5 % cases. Another study conducted by Daniels E et al. and Lewallen S et al. showed 6.6 % and 34.5 % respectively.[6,12]

Pterygium was found in 12.5 % cases but it was more in Daniel E et al. study 13 (21.7 %).[12]

Parikh R et al. the survey was conducted on leprosy patients and found that potentially sight threatening (PST) pathologic features (corneal anaesthesia, lagophthalmos, uveitis, scleritis, and advanced glaucoma) were present in 10.4 % of patients. Significant cataracts occurred 3 times more frequently in those with polar Lepromatous Leprosy.[10]

None of the study had reported regarding Nystagmus and afferent pathway involvement in leprosy cured patients but we had one patient having nystagmus with Exotropia. On doing VEP we found afferent pathway defect which was more in right eye than left eye.

| Ocular Manifestations | Daniel E et al. | Lewallen S | Present Study |
|---|---|---|---|
| Lagophthalmos | 1.6 % | 15.8 % | 25 % |
| Keratitis | 6.6 % | 20.1 % | 12.5 % |
| Iris atrophy | 3.3 % | | 12.5 % |
| Cataract | 6.6 % | 34.5 % | 37.5 % |
| Pterygium | 21.7 % | | 12.5 % |
| Visual acuity 6/60 or less | 8.3 % | | 20 % |

***Table 3. Comparing the Different Study on Ocular Manifestations of Leprosy***

## CONCLUSIONS

Ocular manifestation is higher among male patients and in older patients of > 50 years of age. So, there is a need to create awareness of ocular involvement in leprosy patients to prevent long term visual loss. All patients require regular ophthalmic examination and should be conducted in all active and even after completion of treatment for leprosy for rest of their lives.

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