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REVIEW PAPER ON LEPROSY

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ABSTRACT

Leprosy is also known as Hansen's disease, is a chronic infectious disease caused by Mycobacterium leprous, a microorganism has predilection for the skin and nerves. The disease is clinically characterized by one or more of the three cardinal signs Hypo pigmented or eythematous skin patches with definite loss of sensation, thickened peripheral nerves, and acid fast bacilli detected on skin smears or biopsy material. M.leprae primarily infects Schwann cells in the peripheral nerves system leading to nerve damage and the development of disabilities.[1] Leprosy is a disease with crippling consequences, not only on the effected person and family but also on the society as a whole. It was considered incurable before the introduction of multi –drug therapy, popularly known as MDT. Detecting new cases and monitoring disabilities caused by leprosy will be a challenge.[2] The state of Ceará ranks 13th in number of cases of leprosy in Brazil, and fourth in Northeastern region, with an average of 2,149 new cases diagnosed every year. This study aimed to evaluate the knowledge of leprosy patients regarding treatment, and to assess the level of treatment adherence and its possible barriers. The study was conducted in the reference center for dermatology, from September 2010 to October 2010, in Fortaleza, Ceará. The study data were collected by means of a structured interview, along with the Morisky-Green test, in order to assess treatment adherence and barriers to adherence. A total of 70 patients were interviewed, out of whom 66 were new cases. The majority of patients were between 42 and 50 years old, and 37 (52.9%) were male. Most patients were clinically classified as presenting multibacillary leprosy (80%), and 78.6% of them were from Fortaleza, Brazil. The Morisky-Green test indicated that 62.9% of patients presented a low level of adherence ($p < 0.005$), despite claiming to aware of the disease risks. However, it was observed that 57.1% of the patients had no difficulty adhering to treatment, while 38.6% reported little difficulty. This

study shows that despite the patients claiming to be familiar with leprosy and its treatment, the Morisky-Green test clearly demonstrated that they actually were not aware of the principles of therapy, which is evidenced by the low degree of treatment adherence.[26]

KEYWORDS: Leprosy.

INTRODUCTION

Leprosy is a chronic infectious condition caused by mycobacterium leprae (M.leprae).

It is endemic in many regions of the world and a public health problem in Brazil.

Additionally it presents a wide spectrum of clinical manifestations which are dependent on the interaction between M.leprae and host, and are related to the degree of immunity to the bacillus.

The diagnosis of this disease is a clinical one.

However, in some situations laboratory exams are necessary to confirm the diagnosis of leprosy or classify its clinical form.

Leprosy is cured by multidrug therapy regimens are applied according to the operational classification established by world health organization (WHO).

The drugs used in treatment are usually well tolerated and cases of relapse disease are rare.[3]

The disease that is most familiar with as leprosy is result of a bacterial infection.

M. leprae belongs to the same genus as the bacterium that causes tuberculosis.

Like tuberculosis, M. leprae is an obligate intracellular parasite in humans.

It preferred host cells are nerves, muscle cells, and skin macrophages.[4]

Visual impairment or blindness is a frequent complication of leprosy.

Blindness results either from mycobacterial infiltration and inflammation of structures in the anterior segment of the eye or from tropic changes following damage to the trigeminal and facial nerves, resulting in lagophthalmos, deformed eyelids or corneal anesthesia.[5]

Leprosy is spread between people. This is thought to occur through a cough or contact with fluid from the nose of an infected person.

Leprosy occurs more commonly among those living in poverty.

Contrary to popular belief, it is not highly contagious.

The two main types of disease are based on the number of bacteria present: paucibacillary and multibacillary. The two types are differentiated by the number of poorly pigmented, numb skin patches present, with paucibacillary having five or fewer and multibacillary having more than five.

The diagnosis is confirmed by finding acid base bacilli in a biopsy of the skin or by detecting the DNA using polymerase chain reaction.

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Leprosy has affected humanity for thousands of years. The disease takes its name from the Greek word while the term "Hansen's disease" is named after the Norwegian physician Gerhard Armauer Hansen. Separating people by placing them in leper colonies still occurs in places such as India, China, and Africa.

However, most colonies have closed, since leprosy is not very contagious. Social stigma has been associated with leprosy for much of history, which continues to be a barrier to self-reporting and early treatment.

Some consider the word "leper" offensive, preferring the phrase "person affected with leprosy". It is classified as a neglected tropical disease. World Leprosy Day was started in 1954 to draw awareness to those affected by leprosy.

Types *of Leprosy*

There are two main types of leprosy

1. Tuberculoid leprosy

It is characterized by lesions in the skin (especially nose and outer areas) and in superficial nerve endings.

The lesions are known as maculae.

There is usually no loss of sensation on the face because of the abundant sensory innervations there.

This form is associated with anhydrosis and loss of adnexal structures.

Because the patient is immunocompetent lesions are not usually large or numerous, and this type of leprosy may resolve spontaneously if the host's immune system is strong.

This kind of leprosy occurs in individuals with effective immune responses and develops delayed hypersensitivity, which can be shown by skin test with lpromin.[6]

The typical axonal damage that occurs in tuberculoid leprosy is the result of infiltrating inflammatory cells and granuloma. It is multifocal and often leads to a total obliteration of fibers.

The thickened perineum contains inflammatory infiltrates and often becomes fused to the epineuria.

The granuloma is made up of epitheloidhistocytes multinuclear plasma cells and lymphocytes.

Frequently, nerves become caseated.

Old lesions show hyalinized fibrotic fascicles with only a few intact axons.

Sensory losses are confined to areas of rash but are followed by multiple mono neuropathies, with large nerve sensory and motor involvement.

The nerves affected are primarily the pressure/trauma dependent nerves, with the ulnar nerve involved in most sural, radial and branches of the facial nerve.

There can be ulnar and posterior auricular nerve thickening, ulnar nerve abscesses and painless injuries.[7]

- ***2. Lepromatous leprosy***

The lepromatpus pole of the spectrum is characterized by confluent papules and nodules, possibly resulting in marked, diffuse infiltration of the skin and giving rise to leonine facies and madarosis.

Lesions are usually symmetrical and bilateral. Early in disease the skin appears infiltrated and waxy.

This pole of the leprosy spectrum is characterized by greater nerve involvement and more server disability.

Nodular and diffuse forms of lepromatous disease have been observed.[6]

Early in disease course, the palms and soles of the feet and deep tendon reflexes are spared.

Later, large nerve trunks become involved, and symptoms extend to the cool surface of the face, corneal anesthesia, with impaired closure of the eyes can lead to painless ulcers.

Primary damage of the nerve is the result of direct infiltration of the organism into macrophages, Schwann cells, perineural cells, fibroblasts, endothelium and infrequently the axons.

Foamy cells ate the result of macrophages and Schwann cells filled with bacillus and other debris.

At least two of the following findings have to be present for clinical diagnosis of leprosy

1. A characteristics patch or skin lesion with impaired sensations
2. A thickened or tender cutaneous or peripheral nerve with impairment of sensations in the area supplied by it.
3. Acid fast bacteria in the skin smear.[8]

- ***Causative Agent of Leprosy***

Leprosy is caused by the bacterium mycobacterium leprae.

It is not very contagious and it has a long incubation period, which makes it hard to low where or when someone caught the disease.

Children are more likely than adults to get the disease.[9]

- ***About Micobacterium Leprae***

Classification of mycobacterium.

Table no. 01.[5]

Kingdom	***Bacteria***
Phylum	*Actinobacteria*
Order	*actinomycetales*
Suborder	*corynobacterineae*
Family	*mycobacteriaceae*
Genus	*mycobacterium*

- Leprosy disease is caused by mycobacterium leprae discovered in 1873 by armauer Hansen in Norway.

- It is acid fast bacilli and staining by ziehl-neelsen method the organism appears rod shaped and deep pink in colour.
- M.lepraehave epidemiological importance.

1. Man is the known host.
2. Optimal growth of organism occurs at 30degree Celsius. This explains its predilection for the skin and upper respiratory track.
3. **Stability:** It remains viable outside the body for several days particularly under humid conditions.
4. **Slow growth:** The generation time of the organism is 12 to 14 days. Making the slowest growing bacterial pathogen.this explains the prolonged incubation period and the protracted course of the illness.
5. **Antigen city:** It shares common antigenic determinants with many other micobacteria.[6]

- The bacterium is rod shaped which can develop only on certain human cells.
- Actually the bacterium enters into the skin of the person and takes long time for incubation.
- Children and people with weakened immunity have more chances to get this disease.
- However this disease is not contagious as believed by many people.[12]
- An intracellular, acid-fast bacterium, *M. leprae* is aerobic and rod-shaped, and is surrounded by the waxy cell membrane coating characteristic of the genus *Mycobacterium*.
- Due to extensive loss of genes necessary for independent growth, *M. leprae* and *M. lepromatosis*are obligate intracellular pathogens, and uncultivable in the laboratory, a factor that leads to difficulty in definitively identifying the organism under a strict interpretation of Koch's postulates The use of monoculture-based techniques such as molecule genetics has allowed for alternative establishment of causation.
- While the causative organisms have to date been impossible to culture *in vitro*, it has been possible to grow them in animals such as mice and armadillos.
- Naturally occurring infection also has been reported in nonhuman primates, including the African chimpanzee, sooty manage, and cynomolgus macaque, as well as in armadillos and red squirrels.
- Red squirrels (*Sciurus vulgaris*) - a threatened species - in England were found to have leprosy in November 2016. However, no squirrel cases have spread to a human for hundreds of years.

Symptoms

- The main symptoms of leprosy include
- Muscle weakness
- Numbness in the hands, arms, feet, and legs
- Skin lesions
- The skin lesions have decreased sensation to touch, temperature, or pain.
- They don't heal after several weeks and are lighter than your normal skin tone.[13]
- Once infected with the mycobacterium the average incubation period is two to three years, but it can range from 6 months to 40 years or longer.
- In 90% of patients the first sign of the disease is feeling of numbness, which may precede the skin lesions by a number of years.
- Temperature is the first sensation lost, followed by light touch, pain and then deep pressure, sensory loss usually begins in the extremities.
- The first skin lesion is usually the indeterminate type, which causes one or a few hypo pigmented spots before evolving into the borderline, tuberculosis or lepromatous types.[14]
- Some symptoms may include
- Growths on skin
- Numbness or lack of feeling in the hands, arms, feet and legs
- enlarged nerves (especially around the elbow and knee)
- nosebleeds and a stuffy nose
- Lesions on the body that are not as sensitive to touch, heat or pain
- Skin lesions that are lighter than the person's normal skin color
- Lesions that do not heal after several weeks to months
- Ulcers on the soles of feet
- Thick, skiff or dry skin
- Server pain
- Muscle weakness or paralysis
- Eye problems that may lead to blindness.[15]

Mode of Transmission

- *Humans* are only significant reservoir.
- Infection probably spreads predominantly from nasal secretions of the case to the skin and respiratory tract of another person.

- Other respiratory secretions and open-skin lesions may also transmit infection transmission requires close contact.
- Although the bacillus can survive up to 7 days in dried nasal secretions, indirect transmission is through unlikely.
- Tran placental transmission is probably responsible for cases under 1 year age.[16]
- Researchers suggest that m leprosy is spread person to person by nasal secretions or droplets.
- However the disease is not highly contagious like with flu.
- They speculate that infected droplets reach other people nasal passages and begin the infection there.
- Some investigators suggest the infected droplets can infect others by entering breaks in the skin
- M. leprosy are apparently cannot infect intact skin.
- Rarely, humans get leprosy from the few animal species mentioned above.
- Occurrence in animal makes it difficult to eracdicateleproy from endemic sources.
- Routes of transmission are still being researched for leprosy.
- Recent genetic studies have demonstrated that several genes are associated with an increased susceptibility to leprosy.
- Some researchers now conclude that susceptibility to leprosy may be partially inheritable.[17]
- The mode of transmission is not clearly established.
- The organism is probably transmitted from person to person by aerosol, with a high subclinical rate of infection.
- Household and prolonged close contact seems important.
- There is anecdotal evidence that it may rarely be transmitted by inoculation, such as by contaminated tattoo needles.[18]

Prevention

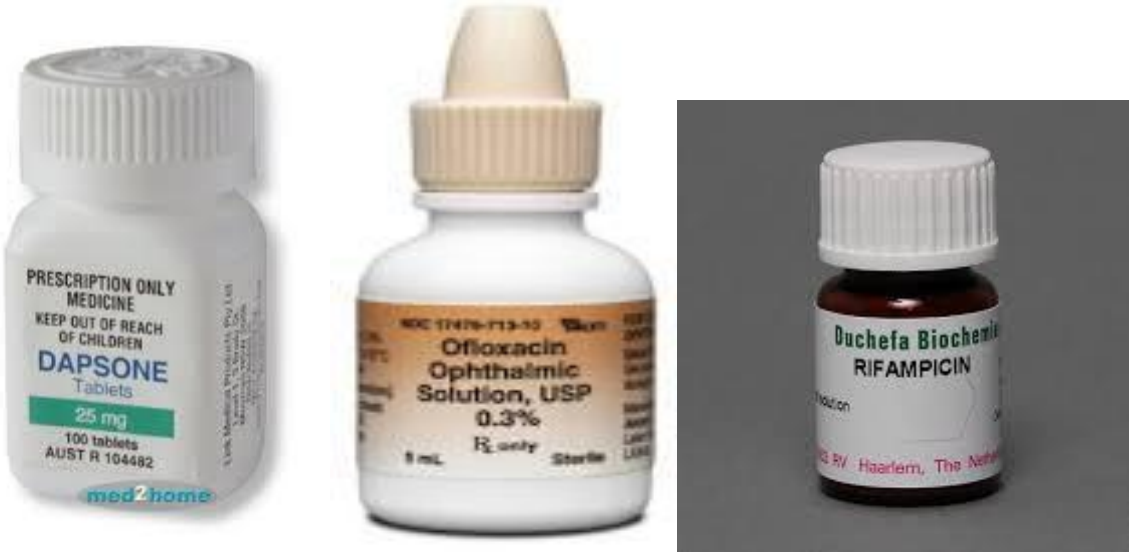
The prevention of leprosy ultimately lies in the early diagnosis and treatment of those individuals suspected or diagnosed as having leprosy, thereby preventing further transmission of the disease to other.

- Public education and community awareness are crucial to encourage individuals with leprosy and their families to undergo evaluation and treatment with MDT.

- Household contacts of patients with leprosy should be monitored closely for the development of leprosy signs and symptoms.
- A study demonstrated that prophylaxis with a single dose of rifampicin was 57% effective in preventing leprosy for the first two years in individuals who have close contact with newly diagnosed patients with leprosy.
- There is currently no wide used standard for using medications for prevention of leprosy.
- Currently, there is no signal commercial vaccine that confers complete immunity against leprosy in all individuals.
- Several vaccines, including the BCG vaccine provide variable levels of protection against leprosy in certain populations.[19]
- Individual should avoid close, long term contact with who have lepromatous leprosy.
- Patient should also avoid touching armadillos because some carry mycobacterium leprous. For this reason, individual should also avoid eating undercooked armadillo.
- Patients who have symptoms of leprosy should seek prompt medical treatment.[20]

Treatment

- Leprosy is usually treated with oral antibiotics for six months to two years, although the duration of treatment depends on clinical circumstances and the choice of regimen.
- Several drugs are used in combination of multidrug therapy (MDT).
- Diaphone, which is bacteriostatic or weekly bactericidal against M. leprous, was the mainstay treatment for leprosy for many years until widespread resistant strains appeared.
- Combination therapy has become essential to slow or prevent the development of resistance.
- Rifampicin is now combined with dapsone to treat paucibacillary leprosy.
- Rifampicin and clofazimine are now combined with dapsone to treat multidrug leprosy.
- A single dose of combination therapy has been used to cure single lesion paucibac illaryleprosy: rifampicin (600mg), ofloxacin (400mg), and minocycline (100mg).
- The child with a single lesion takes half the adult dose of the 3 medications.[21]



(a) (b) (c)

Fig. (a),(b) & (c)- medicines used for leprosy treatment.

- **Treatment summary**

Table no. 02.[22]

Drug name	Adult dose	Pediatric dose	Precautions
Dapsone: bactericidal	100mg/day orally for 6 months for PB leprosy and for MB leprosy 100mg/day orally for 24 months	1-2mg/kg/day orally	Perform weekly blood count. Then perform white blood cell count monthly, then semiannually; discontinue if significant reduction of platelets, leukocytes occur.
Rifampin : For in combination with at least 1 other antituberculous drug. Treat for 6-9 months or until 6 months	PB leprosy: 600mg/month orally or one fourth for 6 months MB leprosy: 600mg/month orally	10-20 mg/kg orally; not to exceed 600 mg/day	If patient has liver disease serious health risks occur such as cerebral hemorrhage or death; may cause red orange discoloration or urine, feces, saliva, sweat, sputum and tears.
Clofazimine: inhibit microbial growth, binds preferentially to mycobacterium DNA. Has antimicrobial properties	50mg/day orally for 24 months in combination with dapson and rifampin.	1 mg/kg/day orally in combination with dapson and rifampin.	Patients should be warned that clofazimine may discolor skin, body fluids, and excrement: color ranges from pink to brownish black; caution in patients with GI problems; skin discoloration due to drug may result in depression or suicide; apply to skin for dryness.

Ayurvedic cure for leprosy

- In Ayurveda, leprosy known as kushtaroga. Leprosy is a chronic disease. this affects particularly the mucous membranes if the nerves and skin.
- Medicines and prescription

Table no. 03: Ayurvedic cure of leprosy.[23]

Medications	***Dose***
khadradirishta	25ml to be taken with lukewarm water after meals daily
Rasamanika, panchanimbachrna, gandhakarasayana	125mg of rasamanikya, 1 gm of panchnimbachrna and 500mg of gandhakarasayana to be taken in the morning and evening.
Mahatiktakaghrita, navakakashaya	10ml of mhatiktakaghrita and 60ml of navakakashaya be taken twice daily.

Diet for Leprosy Patients

- Consumption of vitamin A rich food is very helpful to improve and healing the skin lesions. Carrots, broccoli, cabbage, sweet potato, beet root, red pepper, butternut, spinach, liver lettuce, apricots are much preferred.
- Vitamin B complex rich food is highly recommended to treat leprosy symptoms. Some of the very rich vitamin B complex foods are cheese, beef, octopus, lobster, lamb, fish, eggs etc.
- Vitamin C foods are helpful to strengthen the immune system of the body. Kiwi fruit, guava, orange, lemons, grapes, bell pepper. Garden cress, sprouts, papayas etc, are vitamin C rich foods.
- Foods containing minerals must be added in diet. Zinc and calcium are highly beneficial. Soy milk, cottage cheese, dark chocolate, watermelon seeds, yogurt, salmon, tofu etc are rich in minerals.
- Vitamin D foods like cat fish, button mushrooms, herring, tuna fish, mackerel, and cod liver oil are good for leprosy patients.
- Vitamin E rich foods are good for epidermal cells which improves the skin texture. the skin lesions can be healed naturally by vitamin E rich foods like bell peppers, Swiss chard, mustard green, seeds of sunflower, asparagus.
- Vitamin E improves the epidermal cells by regenerating new cells.[24]
- Essential oils for leprosy –

1. *Frankincense* – smells warm and nice, and it may be applied topically to the skin
2. *Oregano oil* –it might have antibacterial and anti fungal properties
3. Lavender oil – essential oil have inflammatory and sedative properties that can manage the symptoms of leprosy.
4. Thyme and garlic oil – it is an powerful antibacterial agents.[25]

Role of the pharmacist in leprosy

- To describe the role of the clinical pharmacist in a leprosy disease clinic and to describe the development, validation, and operation of the diapason compliance monitoring program.
- Leprosy remains a major, worldwide healthcare problem. Diapason is the drug of choice for treatment of leprosy; however, high rates of noncompliance with this agent have been reported by many treatment centers. The assessment of compliance in leprosy patients is important to help distinguish between treatment failure secondary to noncompliance or to the development of resistance.
- The clinical pharmacist should provide a variety of clinical services in the clinic as well as co-coordinating the clinical research program.
- A pharmacist generated diaphone compliance program led to improvement in compliance rates and clinical outcome.
- The improvement in compliance has been sustained over an extended period of time.
- The clinical pharmacy services performed in the leprosy clinic provide a model for pharmacy involvement in other chronic disease states.
- The dapsone compliance program has been successful in improving patient care and obtaining reimbursement for clinical pharmacy services.[26]
- Pharmacist should use sterile procedure, surgical washing hand
- They should have to choose the therapy according to the patient pathology.
- They should follow right dosage, correct time, time frequency and right way of submitting charge doses.
- New drug, research, industries strategy; discovering new molecules.
- Health nation and local policy.
- They have always active and should formulate new dosages for treatment of leprosy patient.[26],[27]

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