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Mycobacterium leprae and Leprosy: A Compendium

Sumit V. Talwekar [1,*], Neha L. Zod [2], Nikita V. Mahalle [2] and Harigopal S. Sawarkar [3]

[1] *Student of Final Year, Dr. Rajendra Gode College of Pharmacy, Amravati-444602, Maharashtra (India).*
[2] *Department of Pharmacology, Dr. Rajendra Gode College of Pharmacy, Amravati-444602, Maharashtra (India).*
[3] *Department of Pharmaceutical Chemistry, Dr. Rajendra Gode College of Pharmacy, Amravati-444602, Maharashtra (India).*

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Abstract

Leprosy or the Hansen disease is a chronic infectious disease which is caused by Mycobacterium leprae, which primarily involves the skin, peripheral nerves, eyes, and the respiratory tract. Even though it is treatable, it is a publicly transmitted infection, health issue in the third world countries such as India, Brazil and Indonesia. The disease is transmitted by means of long-term contact with untreated individuals and can damage nerves and result in disability when not treated early, and is caused by contact with untreated people. This review discusses the background history, world and regional distribution, bacteriology and the genetic composition of M.leprae. It further talks about the spectrum of the disease, diagnosis and immune responses that identify disease severity. Multidrug therapy (MDT) is the primary mode of treatment, which cures patients and is successful preventing transmission. Nonetheless, leprosy control is still faced with social stigma and late diagnosis efforts, especially in India. The early detection, rehabilitation, and community awareness should be strengthened cure all the leprosy left and assist the affected persons to be reintegrated into society.

Keywords: Leprosy; *Mycobacterium leprae*; Hansen Disease; Nerve Damages; Multidrug Therapy (MDT); Epidemiology; Diagnosis; Social Stigma; India Public Health

1. Introduction

1.1. Historical and Global Situation

Leprosy is defined as a chronic infectious disease involving mainly the skin, peripheral nerves, and mucosa of the upper respiratory tract and eyes. The organism which causes leprosy-Mycobacterium leprae-was first identified by Dr. Gerhard Hansen of Norway in 1874. Unlike most other bacteria, this organism has never been successfully cultivated outside the human body. [3,4,5,6]

Leprosy has been around for thousands of years and, though rare nowadays, still exists in certain developing countries-primarily warm, tropical areas. People with this disease were avoided and secluded not merely on account of the predilectio for transmission but because it can lead to rather conspicuous disabilities and deformities. In many cultures and religions, wrongly viewed as a curse for sin or bad karma. Even the term "leprosy" comes from a Latin word that means impurity. [3,4,5,6]

In 1991, the World Health Organization (WHO) set a goal to eliminate leprosy as a public health problem by the year 2000. They defined "elimination" as having fewer than 1 case per 10,000 people. By the year 2000, over 640,000 people

* Corresponding author: Sumit V. Talwekar

were still being treated for leprosy, and nearly 680,000 new cases were detected that year. Globally, the average rate was still slightly above the elimination target. [3,4,5,6]

Table 1 Registered prevalence of leprosy and detection rate in the top II countries where the disease is endemic [3,4,5,6]

Country	Registered cases (I January 2000)	Prevalence per 10,000	Cases detected in 1999	Detection rate per 100,000
India	495,073	5.0	537,956	54.3
Brazil	78,068	4.3	42,055	25.9
Myanmar	28,404	5.9	30,479	62.9
Indonesia	23,156	l.l	17,477	8.3
Nepal	13,572	5.7	18,693	78.7
Madagascar	7,865	4.7	8,704	51.6
Ethiopia	7,764	1.3	4,457	6 7.4
Mozambique	7,403	3.9	5,488	28.7
Congo DR	5,031	1.0	4,221	8.6
Tanzania UR	4,701	1.4	5,081	15.4
Guinea	1,559	2.0	2,475	32.0
Total	672,596	4.1	677,086	41.7

Of the 122 countries where leprosy was common in 1985, 98 had reached the elimination goal by 2000, and overall cases had dropped by 86%. However, 24 countries still faced serious challenges. Just 11 of them accounted for 92% of new cases, and within those, India alone made up 80%—making it the biggest concern for controlling the disease. [3,4,5,6]

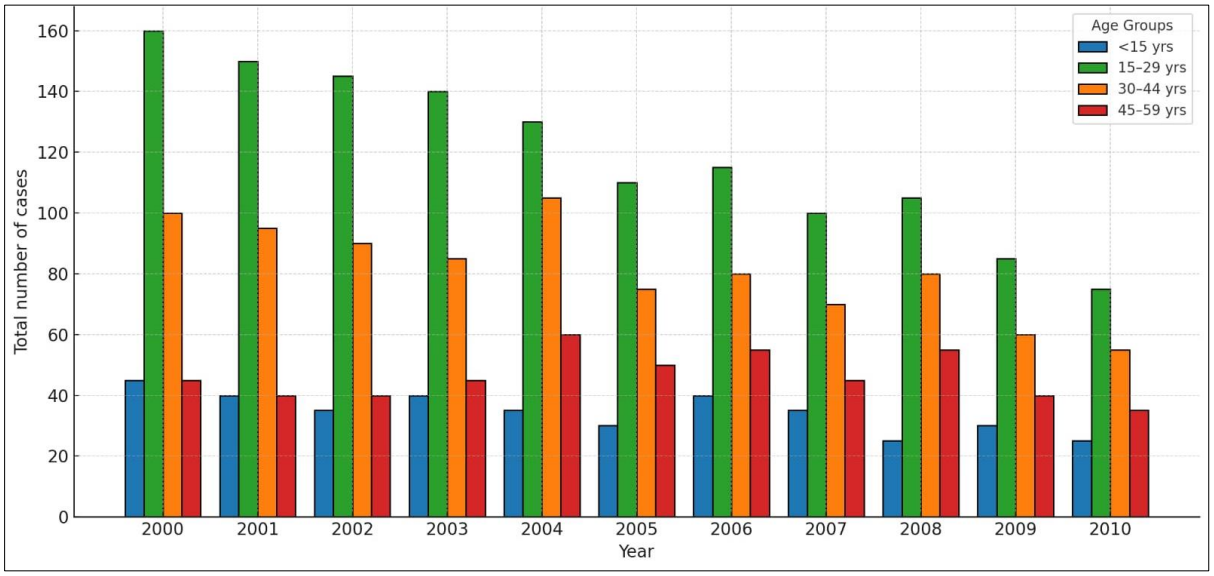

Figure 1 Total number of Cases Leorosy (2000-2010) by Age Group

2. Leprosy: Age, Gender, and Regional Trends

Leprosy affects people of all ages and both sexes, and health programs around the world regularly track patterns in how the disease appears across different groups. These patterns include the type of leprosy (multibacillary or

paucibacillary), whether the person is a child or adult, male or female, and whether they have any disabilities related to the disease. [7,8,9]

In children, both boys and girls tend to show similar types of leprosy. However, in adults, men are more likely than women to have the more severe form (multibacillary). Globally, about 35–37% of all new leprosy cases are found in women. But in some countries, this number is much lower, which raises concerns that many women with leprosy may not be getting diagnosed. This isn't just due to poor access to healthcare other issues like illiteracy, low social status, and cultural barriers also play a role. [7,8,9]

When we look at age, leprosy often shows two peaks: one in the teenage years and another in adulthood. About 9% of new cases are found in children. This is considered a sign that leprosy is still spreading, but numbers can also be affected by how actively schools and families are being screened. [7,8,9]

Leprosy rates also vary a lot from one region to another. South-East Asia reports the highest number of cases, while the Eastern Mediterranean region reports the fewest. In some regions, like the Americas and South-East Asia, there are more new cases reported than existing cases, likely because treatment usually takes less than a year.

Most of the world's leprosy cases come from just a few countries. India, Brazil, and Indonesia alone account for over 80% of new cases every year. In fact, 95% of global cases come from countries that report more than 1,000 new cases annually. These numbers come from data shared by over 100 countries, although the number of countries reporting may change each year. [7,8,9]

3. Bacteriology and Genomics of Mycobacterium leprae

The bacteria that cause leprosy, called Mycobacterium leprae, cannot be grown in a regular lab setting like many other bacteria. Because of this, scientists can't fully apply Koch's postulates (a set of rules used to prove that a specific germ causes a disease). However, M. leprae can grow well in the footpads of nude mice and armadillos, and to a lesser extent in regular mice. Armadillos can also carry the bacteria naturally, and they might help spread leprosy to humans in parts of the southern United States. The disease has also been found in some wild monkeys, which means leprosy can spread between animals and humans—this makes it a zoonotic disease. [10,11,12,13]

Mycobacterium leprae belongs to a group of bacteria called Mycobacterium, which is part of a larger family known for causing diseases like tuberculosis. It only lives and grows inside cells and does so very slowly, taking about 12 to 14 days to divide once. It prefers cooler parts of the body, like the skin and nerves, because it grows best at around 30°C. Outside the body, it can survive for a few days. Its cell wall is thick and complex, which helps it resist certain chemicals and gives it the ability to retain special stains in the lab (making it "acid-fast").[10,11,12,13]

The bacteria have a unique surface glycolipid known as PGL-I. People from endemic areas may develop antibodies against this molecule with or without manifesting the disease. Measuring these antibodies will help to determine who has been infected or is at risk and also to follow treatment progress. However, while helpful in diagnosis, these antibodies do not kill bacteria. [10,11,12,13]

Great advances have come to scientists through genomic study of the bacteria. The full genome of M. leprae has been mapped, and one startling discovery is that so much of its DNA is either not being used or has disappeared. In fact, close to half of its genes are no longer functional and most typical activities are carried out by "pseudogenes," which are dysfunctional copies of genes. Functional genes observed in related bacteria such as the one responsible for tuberculosis. This indicates that M. leprae has lost many functions and now lives by depending on a host, whether human or animal. The paucity of its genetic material is probably the reason it is so slow to grow and why it cannot be kept alive in artificial laboratory conditions. [10,11,12,13]

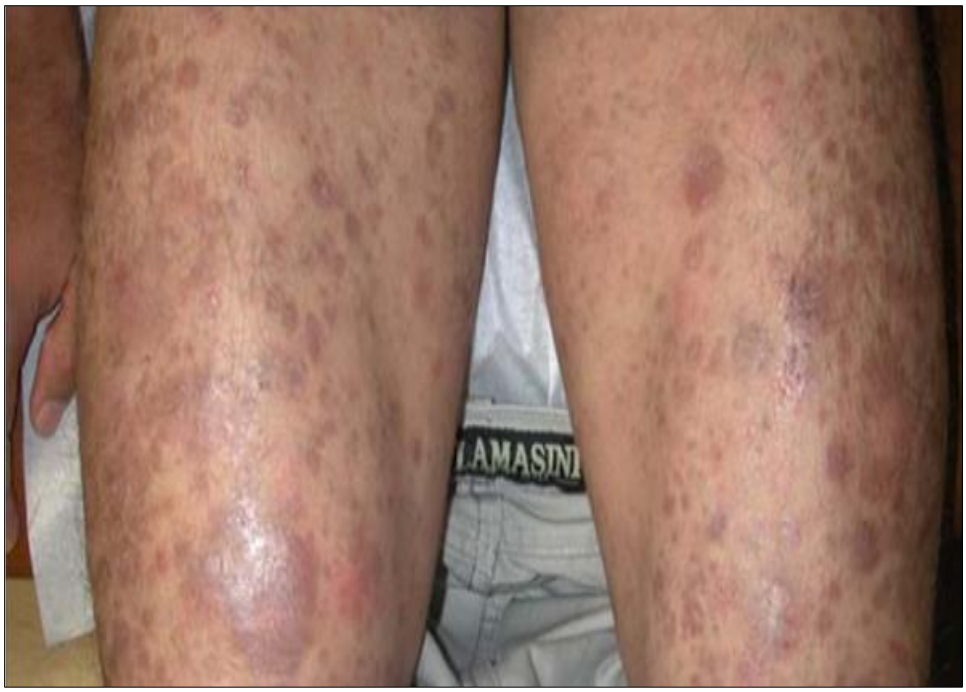

Figure 2 Leprosy case-1

3.1. Leprosy Epidemiology (Especially in Children)

3.1.1. Global Burden

- Over 200,000 new cases of leprosy are reported globally each year (WHO data).[14,15]
- Children account for about 7–10% of new cases annually, indicating active transmission in communities. [14,15]
- The disease remains endemic in parts of: [14,15]
  - South-East Asia (India, Indonesia, Bangladesh)
  - Africa (Brazil, Democratic Republic of Congo, Nigeria, Mozambique)
  - Latin America

3.1.2. Transmission

- Spread primarily through prolonged close contact with untreated individuals via respiratory droplets. [14,15]
- Children are at higher risk due to: [14,15]
  - Close and prolonged household contact with infected adults.
  - Underdeveloped immune systems.

3.1.3. Incubation Period

- Long and variable: 2 to 10 years. [14,15]
- In children, early detection is more challenging because of non-specific signs. [14,15]

4. Disease Spectrum and Diagnostic Procedures

The Mycobacterium leprae bacteria causes Leprosy and although the germ is the same, it is different symptoms which are determined by the strength of a person immunity. There are two types of the disease-tuberculoid and lepromatous that is on the other extreme of the leprosy. [16,17,18]

In the case of tuberculoid leprosy, individuals tend to possess a small number of large, light colored or reddish areas on the skin which are numb, such patches can be scaly with raised edges that are usually well defined. Lepromatous, on the other hand. leprosy diffuses further through the body, and there are lots of spots, bumps or lumps that are red. Sometimes the skin may appear to affect without localities. There are also in between categories of people that can fall into “borderline” categories between these two main types. [16,17,18]

How the immune system of a person reacts towards the bacteria- particularly, with the help of a defense system known as cell-mediated immunity has a significant contribution to the severity of the disease. Individuals who have a higher cell-mediated immunity were more inclined to have the milder form, of tuberculoid, and the individuals with poorer immunity to the severe lepromatous type. [16,17,18]

Scientists have found out that various types of immune messenger molecules (so-called cytokines) are associated with each form of leprosy. In the tuberculoid cases, the IL-2 and interferon-gamma (IFN-g) are produced by immune cells and assist. fight the bacteria. In lepromatous leprosy, the body expression of IL-4, IL-5 and IL- 10 is more associated responses based on antibodies but do not work effectively with these bacteria. This discrepancy is termed as the Th1/Th2 immune response. Th1 cells resist infections within the cells whereas Th2 cells aid in the production of antibodies. [16,17,18]

The special defense system is whereby T cells identify the lipid (fat) molecules of the bacteria instead of protein fragments, unlike the mechanism of many immune responses. Included in a protein known as granulysin. Killing the leprosy bacteria in lab tests has been demonstrated in T cells in tuberculoid lesions. This suggests that granulysin plays a critical role in the body defense against tuberculoid type, particularly in the people. [16,17,18]

The Leprosy is transmitted primarily by minute air droplets carried by expiring, coughing and sneezing individuals. It is believed that nose is one of the major points of entry of the bacteria into the body. A lot of individuals in regions with leprosy common may become a carrier of the bacteria, without showing symptoms. Doctors employ classification systems to learn more about leprosy and diagnose it. The Ridley-Jopling system is

Classified and subdivides the disease into six categories: [16,17,18]

- Indeterminate (I)
- Tuberculoid (TT)
- Borderline tuberculoid (BT)
- Mid-borderline (BB)
- Borderline lepromatous (BL)
- Lepromatous (LL).

This is classified according to the appearance of the skin, involvement of the nerves, and lab tests conducted on tissue samples. However, this system is frequently too complicated to be used in the countries with a shortage of medical resources. [16,17,18]

In order to simplify things, the World Health Organization (WHO) gave a simple technique that only involves two categories: [16,17,18]

- Paucibacillary (PB): five or less skin patches, and no bacteria on skin smears. [16,17,18]
- Multibacillary (MB): on six or more skin patches, bacteria can be observed in smears. [16,17,18]

Generally, the mild or early ones (I, TT, and some BT) are considered PB, whereas advanced cases include (BB, BL, LL, and some BT). Generally, it can be seen that mild or early (I, TT, and some BT) are considered PB, whereas the advanced ones are (BB, BL, LL, and some BT) are MB. [16,17,18]

At a location where the supply of medical personnel is low, a simple flow chart can be employed by doctors to diagnose and categorize patients it does not require sophisticated equipment. In the more advanced nations such as Japan, physicians tend to use the more carry out detailed Ridley-Jopling system and also perform lab tests, such as skin tests and blood tests to, confirm the diagnosis. [16,17,18]

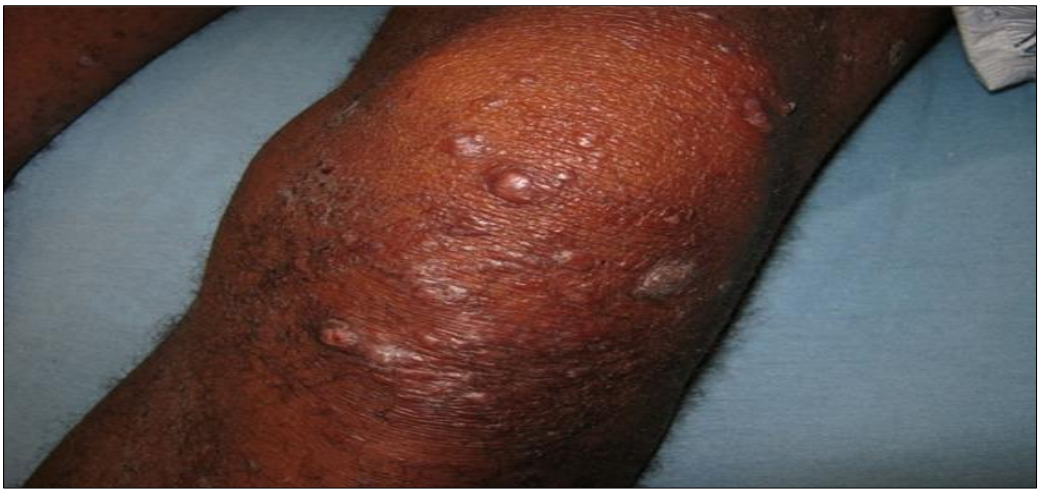

Figure 3 Leprosy case-2

4.1. Leprous Nerve Damage

Leprosy does not only attack the skin, but it also attacks the peripheral nerves or the nerves that are outside the brain and spinal cord. In doing so when the leprosy bacteria attack these nerves, or when the body has an over-active immune. It has the potential to damage nerves, as a result of response to the infection (called a leprosy reaction). This damage leads to loss of sensation, weakness of muscle and other disabilities. [19,20]

The lesions in leprosy of the nerve are termed as mono neuritis multiplex and this implies that multiple individual nerve is affected. The result of this can include issues of feeling (sensory nerves), movement (motor nerves), and automatic body reflexes such as temperature or sweating (autonomic nerves). Some of this, once caught and treated at an early stage, can be cured nerve damage can be reversed. [19,20]

A numb skin patch- an area where the skin appears abnormal is one of the first indicators of leprosy is not sensitive to pain or temperature.

The majority of the severe damage to nerves occurs during what is referred to as a leprosy reaction which is of two types. [19,20]

4.1.1. Type 1 Reaction (Reversal Reaction or RR): [19,20]

In this case, the body immune system becomes very active against the bacteria particularly in the skin and nerves. This is an immune reaction that leads to inflammation that may destroy nerves unless they are treated promptly hence causing permanent paralysis. [19,20]

4.1.2. Type 2 reaction (Erythema Nodosum Leprosum or ENL): [19,20]

Another reaction that also includes inflammation occurs differently and most patients tend to have more severe forms of leprosy. [19,20]

A small fraction (approximately 10 percent) of patients with mild leprosy (PB) and up to a quarter of patients with severe leprosy (MB) have noticeable nerve defects. [19,20]

4.2. How Does the Bacteria Attack Nerves?

The leprosy germ (*M. leprae*) has a special way of attacking the body's Schwann cells, which are the cells that protect and support nerve fibers. It does this using its outer coating, called PGL, which helps it stick to a protein around the nerves known as laminin-2. To make this connection stronger, the bacteria use a small protein called the 21-kDa receptor. Together, this setup allows the bacteria to attach to the Schwann cell surface and slip inside. Once the bacteria are inside, the infected Schwann cells can show pieces of the germ (called antigens) to the body's immune system. This alerts T cells, which then attack the infected Schwann cells. Unfortunately, this attack damages the nerves. On top of that, the body also releases certain chemicals, like TNF-alpha and TGF-beta, during the immune response. These chemicals can harm Schwann cells too—even if the bacteria haven't directly infected them. [21,22]

Treatment and Control Strategy [7.11,14,15,17,20]

Controlling leprosy focuses on three main goals:

- Finding and diagnosing patients early, [7.11,14,15,17,20]
- Giving proper and timely treatment, and [7.11,14,15,17,20]
- Providing full care to prevent disability and help patients recover. [7.11,14,15,17,20]

Since leprosy is an infection, antibiotics are the main treatment. Several medicines work well against the leprosy bacteria, including: [7.11,14,15,17,20]

- Dapsone (DDS) [7.11,14,15,17,20]
- Rifampicin (RFP) [7.11,14,15,17,20]
- Clofazimine (CLF) [7.11,14,15,17,20]
- Ofloxacin (OFLX) [7.11,14,15,17,20]
- Minocycline (MINO) [7.11,14,15,17,20]

These are used in combination, as Multidrug Therapy (MDT) a treatment plan recommended by the World Health Organization (WHO).

Treatment Based on Disease Type: [7.11,14,15,17,20]

4.2.1. Paucibacillary (PB) Leprosy (milder form)

Patients take 600 mg of rifampicin once a month (supervised by a health worker) And 100 mg of dapsone daily (taken at home). This goes on for 6 months. [7.11,14,15,17,20]

4.2.2. Single-lesion PB cases (only one skin patch)

Can be treated with a single-dose combination of 600 mg RFP, 400 mg OFLX, and 100 mg MINO. [7.11,14,15,17,20]

4.2.3. Multibacillary (MB) Leprosy (more severe form)

Patients get 600 mg RFP and 300 mg CLF once a month (supervised) And 100 mg DDS and 50 mg CLF every day at home. This treatment lasts 12 months. Managing Leprosy Reactions: [7.11,14,15,17,20]

Although under treatment, most patients particularly those with borderline or lepromatous forms can develop flare ups of inflammation: leprosy reactions are [7.11,14,15,17,20]

- Type 1 Reaction (Reversal Reaction or RR) occurs in the majority of the borderline cases. [7.11,14,15,17,20]
- Type 2 Reaction (ENL) is more in Lepromatous patients. [7.11,14,15,17,20]

The reactions are capable of destroying nerves fast and hence need to be dealt with instantly and it may be necessary to use corticosteroids to reduce inflammation. In the case of ENL, thalidomide and clofazimine can also be applied.Quick and adequate cure of both infection and reaction is the clue to deterring permanent nerve injury.

4.2.4. Rehabilitation Matters

In case patients are victimized permanently, they ought to be assisted by means of rehabilitation not only to recover the physical wellbeing but also to assist in emotional wellbeing, social or job related wellbeing challenges. Leprosy has the capability of affecting various aspects of the life of an individual; therefore they should be supported in all aspects. [7.11,14,15,17,20]

Can Leprosy Be Prevented? [7.11,14,15,17,20]

A particular vaccine against leprosy is not yet available. Nevertheless, the vaccine against BCG, which is generally applied in fighting tuberculosis, offers some protection. Nevertheless, it does not make sense to run a global BCG campaign purely because of leprosy because of its cost. Scientists are developing a vaccine that is based on DNA and this could be more successful and cheaper in the future. For early diagnosis and appropriate treatment with MDT is now

the greatest weapon we possess to combat leprosy. This remains the global leprosy control core strategy. [7.11,14,15,17,20]

5. Social Impact of Leprosy in India

The history of leprosy in India is long and painful-not to mention as a physical ailment, but as a formidable generator of social stigma. Lepers were excluded, ignored and treated like outcasts in centuries. The fear going around the disease was not only a matter of infection, but a matter of culture, religion and deep-rooted myths. [5,6,7,14,17]

The traditional Indian society used to believe that leprosy was a curse or a penalty of sins in the previous life.This assumption turned this disease not only into a health concern, but a moral and social verdict. People diagnosed families frequently dumped their lepers, withheld their basic rights and sent them out of their homes and villages. Others went to leprosy colonies-distinct settlements in which they could reside among the rest of society, obscured and lost. [5,6,7,14,17]

Even though in 1955, India introduced a national campaign to combat leprosy, and new therapies (such as multidrug or MDT) have taken effect, the incidence of the condition is rising therapy, was made widely accessible as early as the 1980s, the social stigma was still very high. Even after a person they were cured, when they were still frequently discriminated. Symptoms of the disease visible, including deformities of the reintegration into society incredibly hard because of hands, feet or face. [5,6,7,14,17]

This exclusion was reflected and enforced in Indian laws long enough. Over 100 laws discriminated against people affected by leprosy. Having the disease could result in their legal divorce. They were barred from they have to fight elections, they have to ride a transport in this or that place, or even they have to live somewhere. It wasn't until 2019 that the Personal Laws (Amendment) Bill was passed by the Indian Parliament, and at last leprosy was eliminated as a grounds of divorce in five major laws of personality. This was a great stride in the right direction but years later the medical world had already testified that leprosy was neither an evil nor very contagious illness. [5,6,7,14,17]

The cruelty against the human rights was not only legal but also personal. Individuals with leprosy usually struggle with.

lost their jobs, education opportunities as well as social standing. It was even more difficult with leprosy women. A lot of them were left by their spouses, shunned by families, or dragged into poverty and begging. Children of leprosy tended to be bullied at school and they were social stigmas, despite not having the genetic condition completely healthy. [5,6,7,14,17]

Though the government is trying, along with campaigns to address the issue of public health, social fear is deeply rooted in several regions country. This is one of the greatest burdens of the current time because individuals tend to conceal their symptoms due to fear of being rejected. This builds up to late detection and treatment resulting in unnecessary suffering and augmentation of the unnecessary suffering threat of irreversible disabilities. [5,6,7,14,17]

There are over 700 leprosy colonies today in India with many of the cured living in them not because they have to, because they think there is no place they can go out. These colonies are in most cases ill equipped and neglected. Even though there are NGOs and government initiatives that advocate rehabilitation, there is still an actual lack of acceptance in a society slow.

These wrongs have been attempted to be corrected in the past few years. The National Leprosy Eradication Programme (NLEP) still strives to achieve the early detection and awareness of the population. Non-governmental agencies such as

The Leprosy Mission Trust India support, treat, educates, and offers legal assistance to the people affected. Health campaigns and figures in the limelight have attempted to eliminate stigma and stigma and some former patients have become supporters of other rights. [5,6,7,14,17]

6. Conclusion

Leprosy, in spite of being one of the oldest known diseases, still reminds us how science, medicine, and society are closely linked. The cause of Mycobacterium, which is known as Mycobacterium, has been understood over the year leprae, and creating effective drugs such as the multidrug therapy (MDT), that have the ability to cure the disease

completely when given early. But, fighting leprosy is not just a medical struggle but also the struggle to break the walls of stigma, discrimination and fear which are still prevalent in most communities.

India and other endemic countries have done a tremendous improvement in developing reduced number of new cases but still there are still problems with early infection detection particularly in children and women. Awareness, early diagnosis, and sustained public health work will be the determinant of a leprosy-free world.

In the end, the real success will not just be curing the infection. It will be about giving people back their dignity, acceptance, and equal opportunities. With compassion, education, and steady effort, leprosy can be eliminated not only as a disease, but also as a social burden.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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